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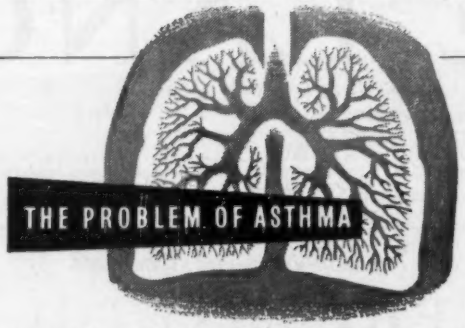

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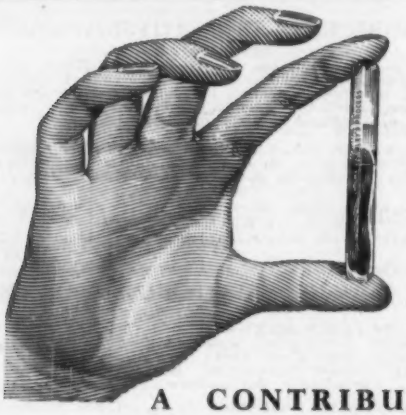

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Marmite yeast extract has been found particularly valuable in the treatment of nervous conditions associated with vitamin B deficiency. It supplies all known factors of the vitamin B complex in a palatable form. Marmite is easily administered, as it can be readily included in the diet.

MARMITE
yeast extract

Literature on request

MARMITE LIMITED, 35 SEETHING LANE, LONDON, E.C.3.
5609

SOUTHON LABORATORIES

ESõBAN OINTMENT

For allergic and industrial dermatoses

Esõban ointment consists of the essential unsaturated fatty acids which promote healthy skin metabolism. It is readily absorbed, self-sterilizing and is an ideal ointment base compatible with the usual medicaments prescribed in Dermatology.

Available in 2 oz. and 16 oz. jars

A product of

SOUTHON LABORATORIES LTD.
LONDON, S.W.15

Southon

Thyrophem *tablets*

A preparation in new form for use under medical advice, in the treatment of adiposity. Invaluable for patients in the mid-forties who find themselves gently putting on weight and quietly losing mental and physical vigour.

Each tablet contains

Dextro-Amphetamine Sulphate 5 mgm.
Thyroid B.P. Gr.¼.

Packed in bottles of 50, 100, 500, and 1000.

write for literature and samples :—

THE ARMOUR LABORATORIES
(ARMOUR & COMPANY LTD.)

Hampden Park, Eastbourne, Sussex
Telephone : HAMPDEN PARK 740 Telegrams : ARMOLAB, EASTBOURNE

HUMANISED TRUFOOD

A MILK MODIFICATION SPECIFICALLY DESIGNED TO MEET THE NUTRITIONAL NEEDS OF THE NORMAL INFANT

Humanised Trufood is not just a dried milk : it is a modification of cows' milk specifically designed to meet the needs of the normal infant from birth.

The fat content compares favourably with that of "Full Cream" dried milk powders. Moreover, as Trufood is dried by the spray process the fat is kept in a fine, well-diffused emulsion, thus ensuring easier assimilation.

Full information about Humanised Trufood and the seven other Trufood milks for infants will be supplied on request to Trufood Limited, 113 Newington Causeway, London, S.E.1.

You will find that when you have to feed an infant artificially there is a better Trufood milk available whatever your requirement may be.

Full information available from Trufood Limited 113 Newington Causeway, London, S.E.1

TRUFOOD

The Trufood Creameries and Laboratories are at Wrenbury in Cheshire

TFD 56-044-100

Availability of Vitamins in Yeast

Deficiencies of single factors of the Vitamin B Group do not occur. Accordingly, even if a deficiency condition appears to result from the lack of an individual factor of the group and it is considered necessary to give intensive treatment with this factor, *the entire Vitamin B Complex should be administered concurrently.*

It is, however, extremely important, in view of suggestions in recent publications, that the vehicle selected as a source of the entire B Complex does not withhold its vitamin content from the patient.

Human experiments show that the rich, natural vitamin potency of Aluzyme is totally available to the human system.

● *Aluzyme is not advertised to the public and may be prescribed on* **form E.C.10.**

ALUZYME
The NON-AUTOLYSED YEAST
with completely available Vitamins

Have you had your free copy of "The Therapeutic and Nutritional Value of Brewers' Yeast"?
Professional Samples and Prices on request from :—

ALUZYME PRODUCTS
PARK ROYAL ROAD, LONDON, N.W.10.

IF THERE IS NO ORGANIC DISEASE TO ACCOUNT FOR

ENURESIS

TREATMENT BY

The "CHIRON" NOCTURNAL ENURESIS ALARM

(PROV. PAT. NO. 16125)

IS INDICATED

THIS TREATMENT IS BASED ON PAVLOV'S THEORY OF CONDITIONED REFLEXES AND HAS PROVED SUCCESSFUL IN 90% OF CASES

SEE *LANCET*, 19 FEB. 55, P. 391 & 26 MAR. 55, P. 676.

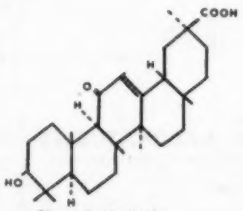
FOR FURTHER INFORMATION WRITE TO:—

DOWN BROS. and MAYER & PHELPS LTD.
Surgical Instrument Makers
32-34, New Cavendish Street, London, W.1
Telephone : WELbeck 3764, 8573.

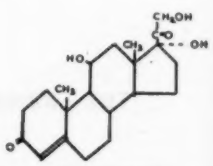
A new anti-inflammatory and anti-pruritic agent

BIOSONE G.A.

BIOSONE G.A. OINTMENTS contain 2% of the dermatologically active isomers of Glycyrrhetinic Acid which, when applied to the skin, has an action resembling that of HYDROCORTISONE (B.M.J. Dec. 1955, p. 1501).



Glycyrrhetic Acid
Glycyrrhetinic Acid



Hydrocortisone

Available in SPECIALLY FORMULATED BASES which take into account the sensitive nature of G.A.:—

BIOSONE G.A. OINTMENT (GREASY)
BIOSONE G.A. Ointment (NON-GREASY)
BIOSONE G.A Ointment with NEOMYCIN

FREELY PRESCRIBABLE ON E.C.10.

BIOSONE G.A. is INEXPENSIVE by comparison with Hydrocortisone and no systemic or local reactions have been reported.

BIOSONE G.A. OINTMENTS

The FIRST CHOICE in the treatment of DERMATOSES

Pack: 25 gm. tubes

Samples and literature available on request.

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Research and manufacture by BIOREX LABORATORIES LTD., 47/51 Exmouth Street (Mkt.), Rosebery Avenue, London, E.C.1.
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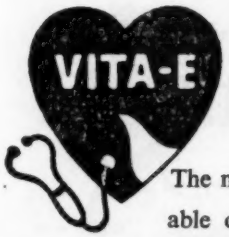


Alpha tocopherol (Vitamin E) for CARDIOVASCULAR-RENAL DISEASES

The natural vitamin E available only since 1948 must not be confused with the wheat germ oil in use before that date with its limitations as to potency and stability.

The natural vitamin E of today comprises a concentrate distilled from the oils of cottonseed, palm, soya bean, etc.

The standard laid down by the League of Nations is that 1 international unit = 1 mgm. of d.l. *alpha* tocopheryl acetate.

The VITA-E Gelucap (75 i.u.) heads the list of brands approved by the Vitamin E Society and is that recommended by the Shute Foundation for Medical Research and used with such conspicuous success at the Shute Institute.

LITERATURE ON REQUEST

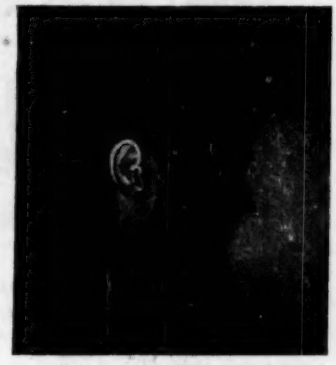
Sole Manufacturers:

THE BIOGLAN LABORATORIES LTD.
HERTFORD, HERTS, ENGLAND.

Specialists in Hormones and Vitamins

EAR WAX *Removed this easy way*

The removal of wax from the external auditory meatus has, in the past, normally entailed attendance by the patient for diagnosis and for the prescription of a suitable loosening agent, and a second attendance a few days later for syringing.
Now, by the use of Cerumol Ear Drops, wax can be removed in most cases at one visit. A few drops of Cerumol can be instilled into the ear and, while another patient is being attended to, the soft cerumen dissolves and the harder wax disimpacts. The wax can then be removed by gentle syringing or with cotton wool. The wax may even be found to run out of the ear on its own accord, in which case patients themselves may instil Cerumol at home, obviating further attendances.
Cerumol is anti-bacterial, non-irritating and harmless to the lining of the external auditory meatus or the tympanic membrane.
Cerumol is included in Category No. 4 of the M.O.H. classified list of Proprietary Preparations and may be prescribed on N.H.S. Form E.C.10.



PACKS:—For Surgery Use: 10 *c.c. vial—separate dropper included. (Basic N.H.S. price* 2/8.) *For Hospital Use:* 2 *oz. and* 10 *oz. bottles.*

CERUMOL
Reg. TRADE MARK

EAR DROPS
for the easier removal of wax

Distributors in U.K.
TAMPAX LIMITED, BELVUE ROAD, NORTHOLT, GREENFORD, MIDDLESEX. Tel.: WAXlow 2244

If you wish to test for yourself and have not received recently a 10 *c.c. vial, please write or telephone direct to:*
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7

Furadantin★

BRAND OF NITROFURANTOIN

in urinary tract infections

Duncan

Furadantin is an antibacterial compound for the oral treatment of urinary tract infections only. Therapeutic concentrations up to 400 mcg./ml. appear in the urine but blood and tissue concentrations are very small. The drug is effective against most organisms found in the urinary tract, including *Proteus* and *Aerobacter*, and some strains of *Pseudomonas*.

Advantages

- Oral administration
- Action confined to urinary tract
- Broad antibacterial spectrum
- Only minor side-effects

Furadantin (brand of nitrofurantoin) is available as tablets of 50 mg. in bottles of 25 or 250.

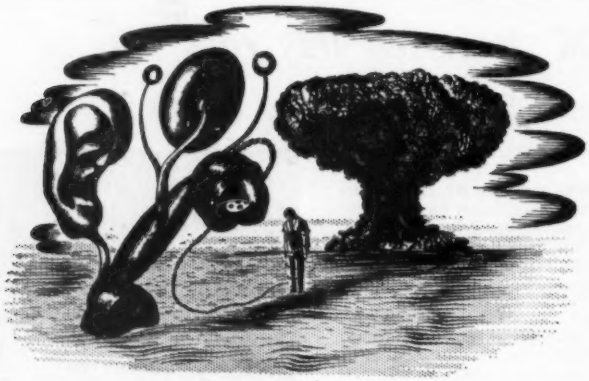
Further information on the use of Furadantin, or Diagnostic Tablets for bacterial sensitivity tests, will be sent on request.

DUNCAN, FLOCKHART & CO., LTD.

16, Wheatfield Road, EDINBURGH, 11

4, Carlos Place, LONDON, W.1

★ *Furadantin is manufactured by a registered user of the trade mark under licence from the Norwich Pharmacal Company (Eaton Laboratories Division).*



BEPLETE

Elixir — Tablets

WINGS DAY SEPT. 15th GIVE FOR THOSE WHO GAVE

Wyeth

The word 'Beplete' is a registered trade mark of

Neurosis Potential

The rush and acceleration of civilisation's headlong dash into the atomic age is bringing the syndrome exemplified by tension, neurosis and stress into ever greater prominence.
BEPLETE provides an effective, short-term method of raising the anxiety threshold. Presenting phenobarbitone in concealed form, (¼ grain to the dose), masked within a tonic cloak of the Vitamin B-complex, it permits successful sedation in the patient with the over-anxious and enquiring mind.

Beplete Elixir is available in bottles of 4 fluid ounces and as Tablets in bottles of 50.

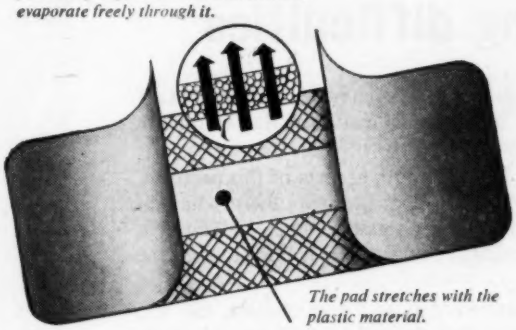
JOHN WYETH & BROTHER LIMITED, CLIFTON HOUSE, EUSTON ROAD, N.W.1

Elastoplast

Airstrip

a waterproof, yet non-occlusive, adhesive first aid dressing that prevents maceration

The plastic material consists of a micro-porous extensible filter, air-permeable yet waterproof. Sweat and skin exudates evaporate freely through it.



The pad stretches with the plastic material.

Elastoplast 'Airstrip' is a new type of first aid dressing. It is made from a specially developed plastic material, through which sweat and skin exudates evaporate at the same rate as they develop on the skin. The material is, in fact, a micro-porous extensible filter, and is not perforated. It provides a barrier to water, grease, oil and infective organisms.

Even after long application, Elastoplast 'Airstrip' does not cause the underlying skin to macerate. The adhesive is specially spread in a lattice pattern so that micro-porosity is retained and firm adhesion not impaired. The surface of the wound and the surrounding skin remain dry beneath an 'Airstrip' dressing, which can be left on until the wound heals.

Full details on application to :—

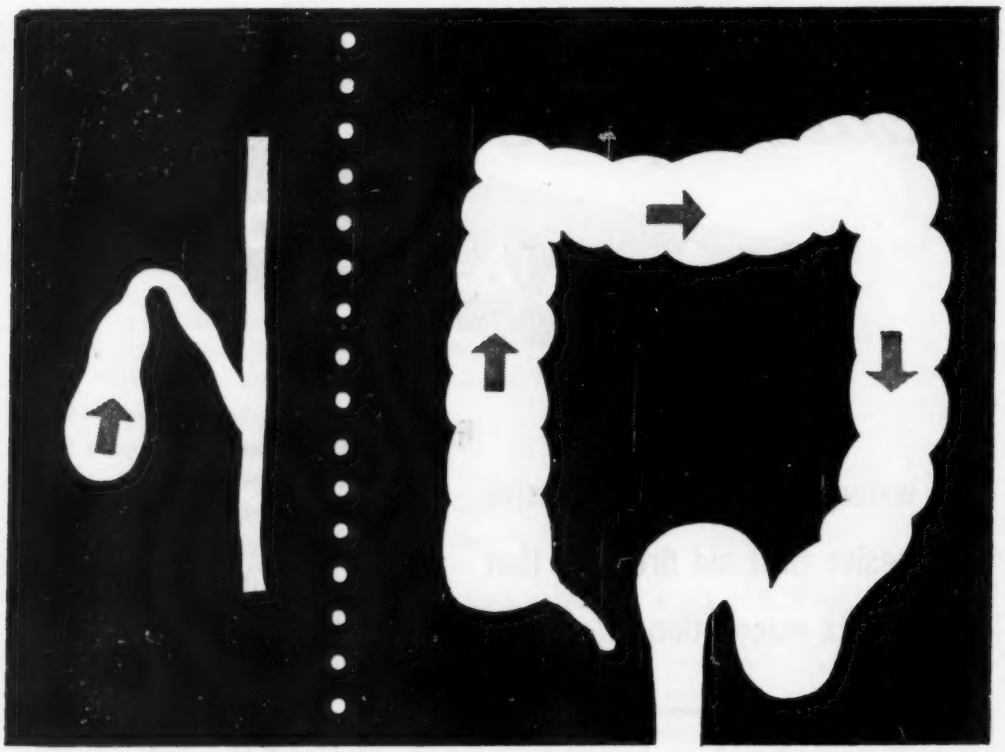
SMITH & NEPHEW LIMITED

WELWYN GARDEN CITY · HERTS

1856 S&N 1956

PROFESSIONAL PACK
available in cartons of:—
100 dressings 1¼″x ⅞″ **9/8d.**
„ „ 2½″x ⅞″ **13/4d.**
50 dressings 1¼″x 1½″ **7/-d.**
„ „ 2½″x 1½″ **10/3d.**
Less the usual professional discount.

PUBLIC PACK
sold by all chemists at **1/-** and **2/-** each.



eliminating difficulties

Difficulties in elimination are often associated with hepatobiliary disturbances. The resultant biliary stasis can itself lead to further intestinal sluggishness.

Veracolate is formulated to deal with both aspects of this problem. First, Veracolate contains bile salts which stimulate the production and flow of bile. Secondly, the phenolphthalein and cascara content of Veracolate encourage intestinal activity—thus helping to void the intestinal contents.

Active principles: Sodium taurocholate and glycocholate, 1.07 gr., ext. cascara sagrada, 1.00 gr., phenolphthalein 0.50 gr., oleoresin capsicum 0.04 gr.

Dose: 1 tablet 3 times a day or 2 at night.

Packing: In bottles of 50 and 100 tablets. Bottles of 500 tablets supplied to chemists for dispensing.

Veracolate

No Warner preparation has ever been advertised to the public.

WILLIAM R. WARNER & CO. LTD., POWER ROAD, LONDON, W.4.

CHEMOTHERAPY OF TUBERCULOSIS

B-PAS WANDER PRODUCTS

These are now in unrestricted supply to provide the significant advantages of the newest clinically proven modification of PAS, i.e. B-PAS (4-Benzoylamino-2-hydroxybenzoic acid).

Extensive published reports based on the criteria of bacteriostatic levels, tolerability and clinical results show that B-PAS (Wander), first introduced by our Research Laboratories in 1948, is a major contribution to tuberculotherapy.

Calcium B-PAS (Wander) is virtually insoluble; hence its slower absorption and excretion, and ability to provide high blood levels of extended duration, but with relatively low dosage. In contradistinction to other forms of PAS, B-PAS (Wander) is entirely free from unpleasant taste. It is thus acceptable to patients in easily taken powder form, as well as in cachets if preferred. The powder form is supplied in convenient single-dose envelopes, or in bulk in any quantity.

PACKS—Powder: Tins of 150 and 500 x 3.5 g. envelopes.
Cachets: „ „ 80 and 400 x 1.0 g.

Sodium B-PAS (Wander) also available in 1.5 g. Cachets

'B-PASINAH' WANDER

combined B-PAS and Isoniazid (INAH)

To facilitate concurrent administration of B-PAS (Wander) and INAH, this product is formulated so that 12 Cachets daily in divided dosage provides 12 g. of Calcium B-PAS (Wander) plus 300 mg. of INAH.

PACKS—Cachets each containing 1 g. B-PAS (Wander) and 25 mg. INAH: Tins of 100 and 500.

Full Abstracts from Literature on B-PAS, also details of institutional quantities and prices sent on request.

All Wander tuberculostatic products may be obtained from usual pharmacists or direct from

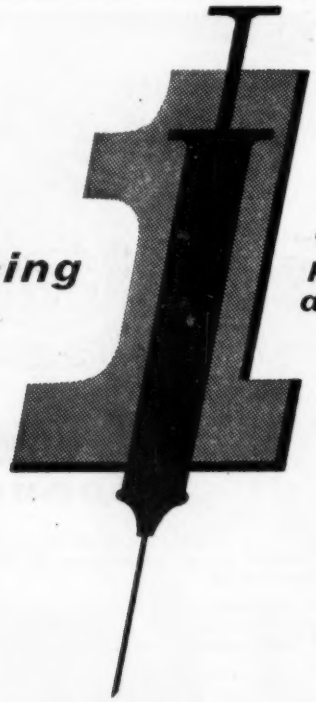
A. WANDER LIMITED

42 Upper Grosvenor Street, Grosvenor Square, London W.1

CANADA: A. Wander Ltd., Peterborough, Ontario. **AUSTRALIA**: A. Wander Ltd., Devonport, Tasmania. **NEW ZEALAND**: A. Wander Ltd., Christchurch. **INDIA**: Khatau Valabhdas & Co., Indian Globe Chambers, Fort Street, Fort, Bombay, 1. **PAKISTAN**: Grahams Trading Co. (Pakistan) Ltd., P.O. Box 30, Karachi. **CEYLON**: A. Baur & Co. Ltd., Colombo.

M396

announcing



the new one-dose post-operative analgesic

PROLADONE

Dihydrohydroxycodeinone pectinate

Clinical trials have shown that, in most cases, satisfactory post-operative pain control is obtained with one injection.

DOSE: *10 ml. by intramuscular injection.*
PACKING: *1 ml. ampoules in boxes of six.*
CLINICAL SAMPLES *are available for trial on request.*
This product is controlled by the D.D.A. Regulations and requests for samples must be worded accordingly.

PROLADONE

TRADE MARK

long acting analgesic

THE CROOKES LABORATORIES LIMITED · PARK ROYAL · LONDON · N.W.10

12

"In these days of economy in prescribing"

Extract from a letter in the BRITISH MEDICAL JOURNAL, August 11th, 1956. p. 374

"A recent annotation in the Journal, on the treatment of constipation, incriminates liquid paraffin as a cause of lipoid pneumonia and as an obstacle to the absorption of fat-soluble substances such as carotene and to the healing of wounds. In these days of economy in prescribing . . . . the biologically standardized form of senna . . . . is cheaper by half than paraffin, is far easier to dispense, and there is no wastage of storage space."*

**Senokot.*

℞ Senokot

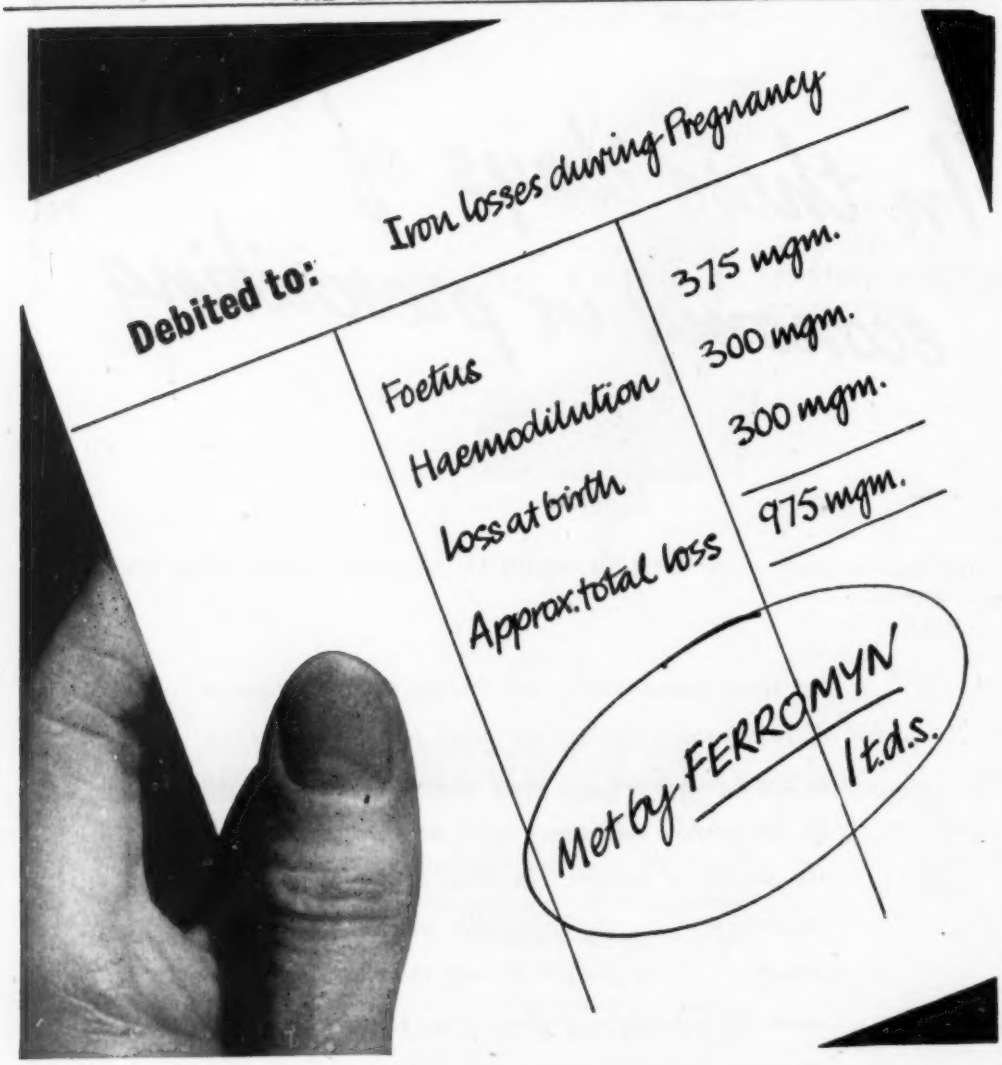
THE FIRST STABLE STANDARDIZED SENNA

Granules: 1-2 teaspoonfuls. Tablets: 2-4

GRANULES: 2 oz., 6 oz. and 2 lb. TABLETS: 50, 200 and 1,000

Prescribed under the N.H.S.: J.C.P. Category 3: no B.P. equivalent; not advertised to the public.

WESTMINSTER LABORATORIES LTD., CHALCOT ROAD, LONDON, N.W.1



PREGNANCY: meeting the inevitable iron deficiency

Progressive inroads are made on the maternal iron stores during pregnancy. The demand made is greatly increased during the third trimester, and there is little doubt that the exposition of a suitable form of iron is of definite clinical value. FERROMYN meets these important demands because it affords maximum bivalent iron from a minimum of ferrous salt, does not cause alimentary upset, has a high utilisation factor and will maintain a satisfactory haemoglobin level throughout term.

FERROMYN is supplied in four forms:

FERROMYN TABLETS Each tablet contains: *Ferrous Succinate 150 mgm.*

ELIXIR FERROMYN Each teaspoonful contains: *Ferrous Succinate 150 mgm.*

FERROMYN 'B' TABLETS Each tablet contains *Ferrous Succinate 150 mgm. Aneurine Hydrochloride 1mgm. Riboflavin 1 mgm. Nicotinamide 10 mgm.*

ELIXIR FERROMYN 'B' Each teaspoonful contains: *Ferrous Succinate 150 mgm. Aneurine Hydrochloride 1 mgm. Riboflavin 1 mgm. Nicotinamide 10 mgm.*

FERROMYN

CALMIC LIMITED, CREWE. *Phone CREWE 3251-5* **LONDON:** *2 Mansfield St., W.1. Phone LANgham 8038-9*

AUSTRALIA: 458-468 Wattle Street, Ultimo, Sydney, N.S.W. **CANADA:** Terminal Buildings, York St., Toronto.

. . leadership in oral-iron therapy

F2

Nobecutane

The sterile plastic dressing for small cuts, abrasions and major surgical incisions

Nobecutane is suitable for dressing most wounds from small cuts, burns and abrasions to major surgical incisions. Its great tensile strength and elasticity make it useful for covering those injuries where the patient can continue at work, for it gives maximum protection with minimum limitation of movement. As it is both waterproof and dustproof, and will withstand most detergents and emulsified oils, it is an ideal industrial dressing, especially where hygiene in the preparation of food is important. As it is impermeable to bacteria but allows normal skin respiration, the dressing ensures healing with no contamination of the wound and no maceration of the skin.

Waterproof
Dustproof
Impermeable to Bacteria
No Wound Contamination
No Skin Maceration

PRESENTATION
100 ml. and 300 ml. spray containers, 50 ml. bottles.

EVANS MEDICAL

EVANS MEDICAL SUPPLIES LIMITED
SPEKE, LIVERPOOL 19 (HUNTS CROSS 1881)
London Office : Ruislip, Middlesex (Ruislip 3333)

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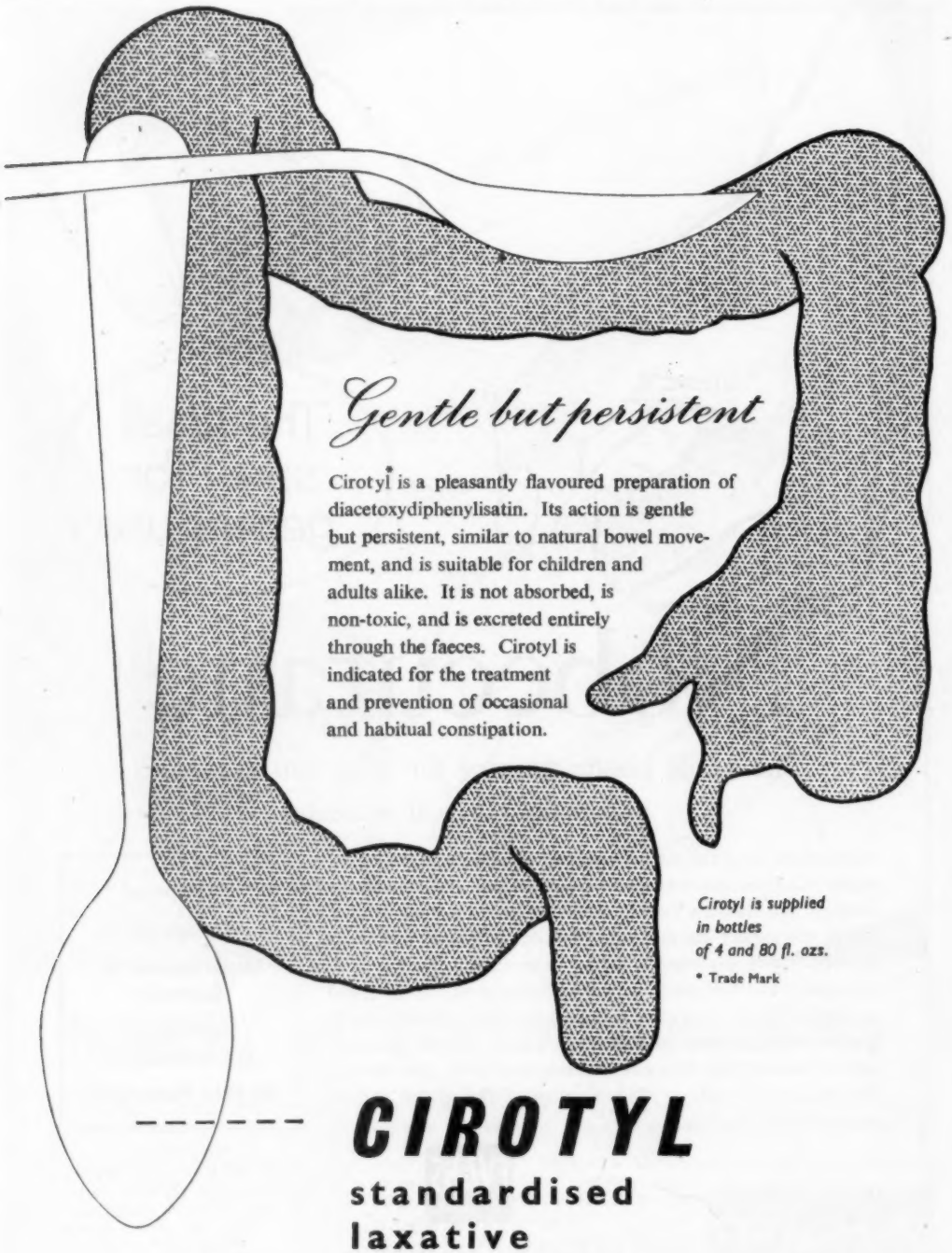


Gentle but persistent

Cirotyl* is a pleasantly flavoured preparation of diacetoxydiphenylisatin. Its action is gentle but persistent, similar to natural bowel movement, and is suitable for children and adults alike. It is not absorbed, is non-toxic, and is excreted entirely through the faeces. Cirotyl is indicated for the treatment and prevention of occasional and habitual constipation.

Cirotyl is supplied in bottles of 4 and 80 fl. ozs.

* Trade Mark

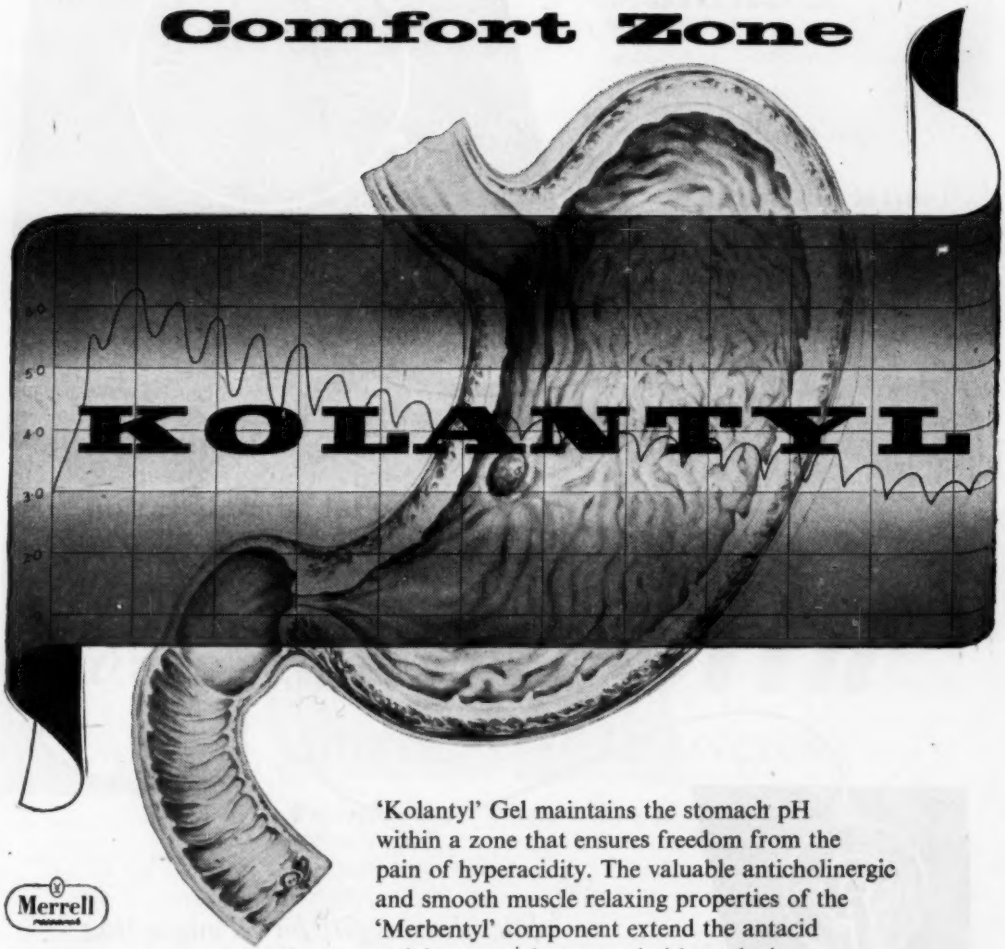
CIROTYL

standardised laxative preparation

PARKE, DAVIS & COMPANY LTD. *(Inc. U.S.A.)* HOUNSLOW • MIDDLESEX • TEL: HOUnslow 2361.
720

Keeping the Peptic Ulcer Patient in the

Comfort Zone



Merrell

Each 10 c.c. of 'Kolantyl' Gel contain:

400 mg.	Dried Aluminium Hydroxide Gel.
200 mg.	Magnesium Oxide.
5 mg.	'Merbentyl'
100 mg.	Methylcellulose
25 mg.	Sodium Lauryl Sulphate.

Tablets containing these ingredients are also prepared.

Availability: 'Kolantyl' Gel is supplied in bottles of 12 fl. oz. 'Kolantyl' tablets in bottles of 50 and 250.

Dosage: 2-4 large teaspoonfuls of 'Kolantyl' Gel (or 2 tablets) three or four times daily. In severe cases a dose may be taken every three hours.

'Kolantyl' Gel maintains the stomach pH within a zone that ensures freedom from the pain of hyperacidity. The valuable anticholinergic and smooth muscle relaxing properties of the 'Merbentyl' component extend the antacid activity over a longer period by reducing peristalsis. This effect is particularly valuable at night. The complementary antacids avoid constipation or undue laxation, and there is no acid rebound.

KOLANTYL GEL

relieves ulcer pain very effectively

distributed in the United Kingdom and Eire by

RIKER LABORATORIES LIMITED, LOUGHBOROUGH, LEICS.

for the Wm. S. Merrell Company, London.

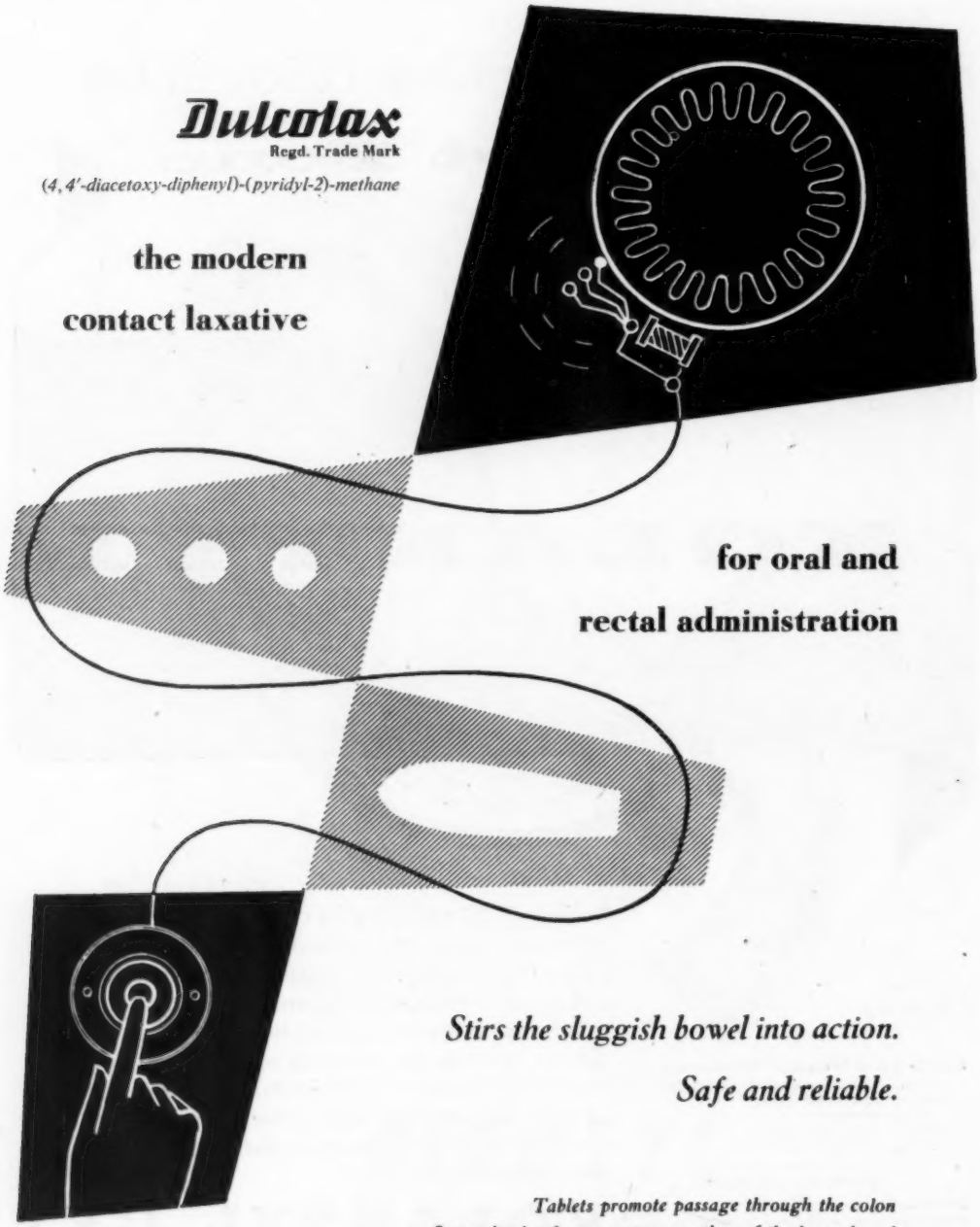
Dulcolax

Regd. Trade Mark

(4,4'-diacetoxy-diphenyl)-(pyridyl-2)-methane

the modern

contact laxative



for oral and

rectal administration

Stirs the sluggish bowel into action.

Safe and reliable.

Tablets promote passage through the colon
Suppositories for prompt evacuation of the lower bowel

Dulcolax enteric coated tablets of 0.005 g. · Bottles of 30 and 200
Dulcolax suppositories of 0.01 g. · Boxes of 6 and 50

LEWIS LABORATORIES LTD., LEEDS 9

NO LONG FACES WHEN CHILDREN TAKE . . .

Maw's

Tancolin (Regd.)

CHILDREN'S COUGH LINCTUS

Active Ingredients	%W/V
Theophylline ...	0.33
Ethylmorphine Hydrochloride	0.025
Sodium Antimonyl Tartrate	0.00125
Ascorbic Acid ...	0.25
Glycerin ...	20.8
Sodium Citrate ...	2.0
Citric Acid ...	1.0

Tangerine Flavoured to provide an immediately acceptable and effective treatment, appealing instantly to even the most unco-operative child patient. Tancolin combines a pleasant vehicle with a rational formulation — specifically for children.

TANCOLIN has been designed to give a twofold anti-spasmodic and sedative action. The inclusion of a demulcent, a reflex expectorant and added Vitamin 'C' content are valuable adjuncts to this primary function.

TANCOLIN is indicated for treatment of the distressing and irritating cough associated with the common cold, Bronchospasm Bronchitis and Inflammatory and Catarrhal affections of the Respiratory Tract.

TANCOLIN is freely prescribable on E.C.10 (Cat. 3/4) and achieves therapeutic efficiency with economy.

S Maw Son and Sons Limited · Barnet · England

G147A

19

The esters of NICOTINIC, SALICYLIC and p-AMINOBENZOIC acids bring relief to cases of arthritis and rheumatism

"Thank you, doctor"

IN CASES OF soft-tissue rheumatism, and arthritic disorders, many doctors are tending more and more to regard Transvasin as an indispensable adjuvant to treatment.

For Transvasin is composed of the esters of nicotinic, salicylic and p-aminobenzoic acids. These esters readily pass the skin barrier in therapeutic quantities, and so enable an effective concentration of drugs to be built up where they are needed.*

Transvasin not only induces vasodilation of the skin with a superficial erythema, but also brings about a deep hyperaemia of the underlying tissues. It is non-irritant and can be safely used on delicate skins.

It is now being widely prescribed, with successful clinical results. Since a very small quantity is sufficient for each application, the cost of treatment is extremely low.

**Therapeutische Umschau VIII, 1952, 10, 143.*

Salicylic acid tetrahydrofurfuryl-ester...	14%
Nicotinic acid ethyl-ester.....	2%
Nicotinic acid n-hexyl-ester.....	2%
p-Aminobenzoic acid ethyl-ester.....	2%
Water-miscible cream base ad	100%

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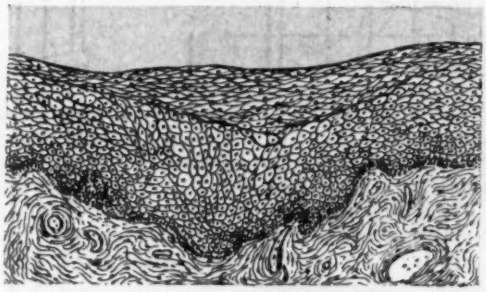
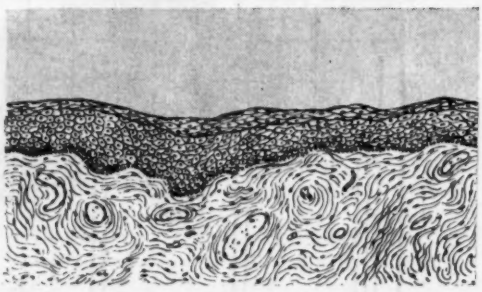
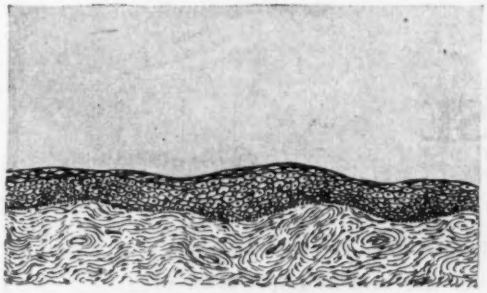


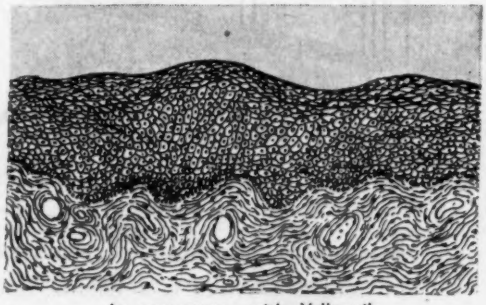
Adult vaginal epithelium maintained by natural œstrogenic activity.



At menopause: reversion of epithelium towards the infantile type.



Post-menopausal, infantile type of epithelium, with thin, atrophic layers.



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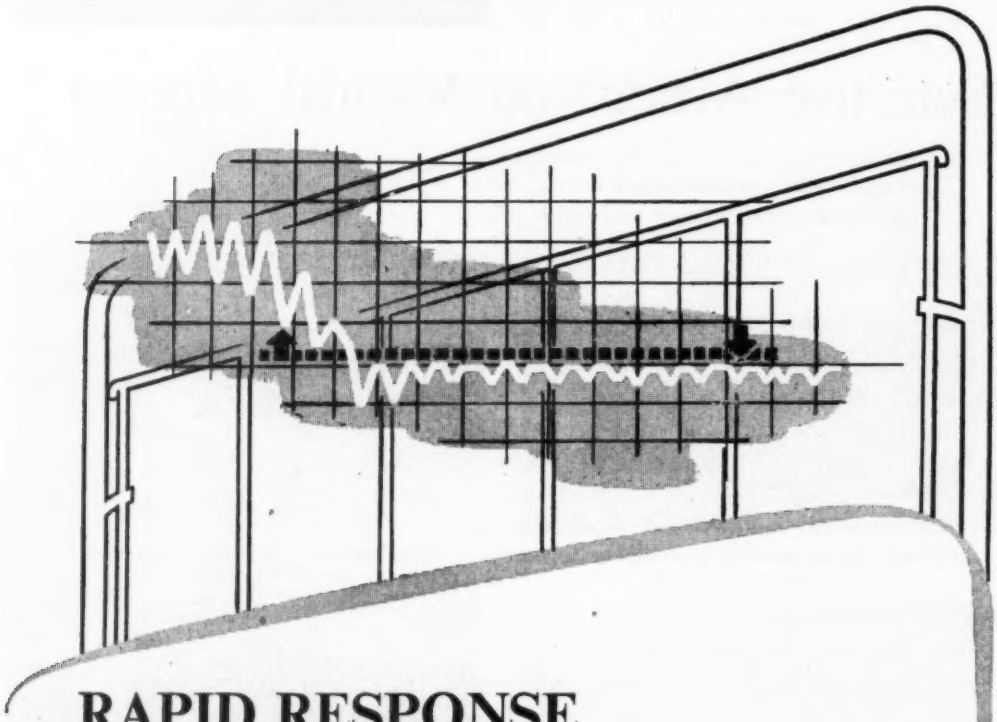

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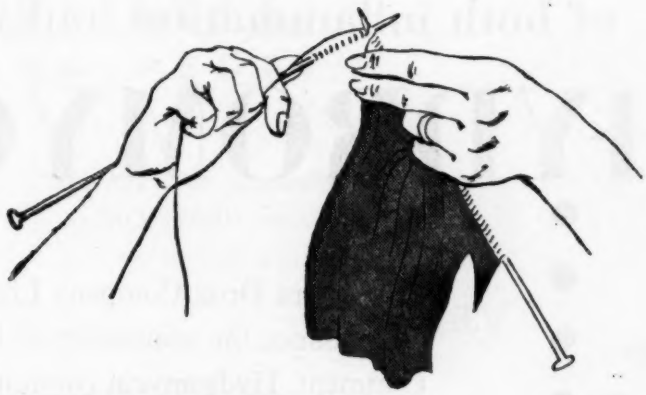

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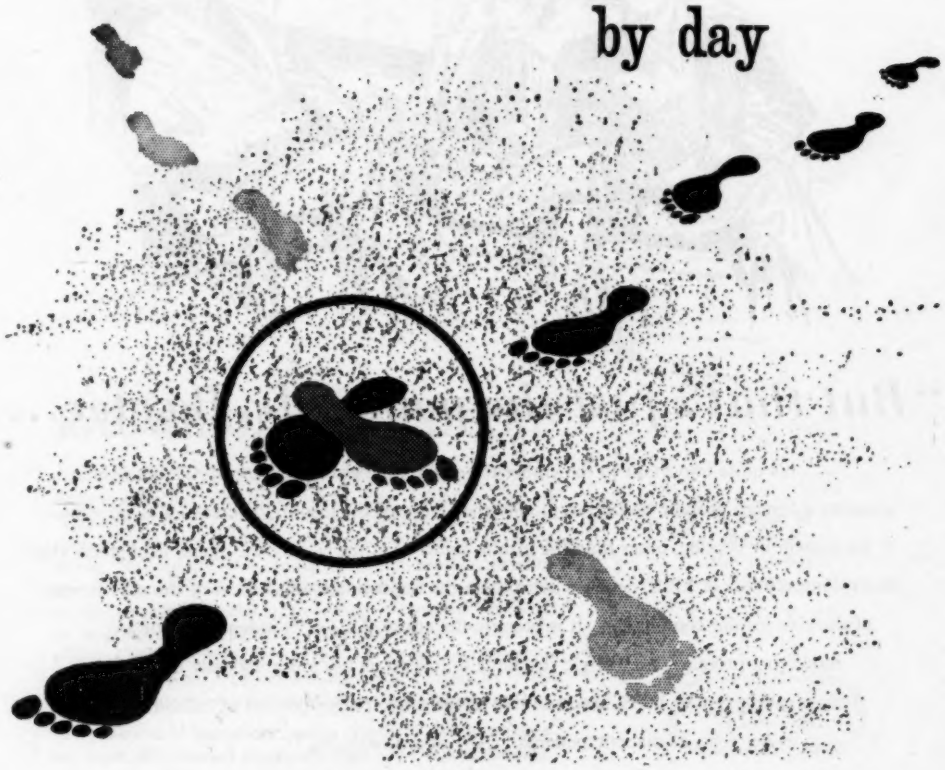

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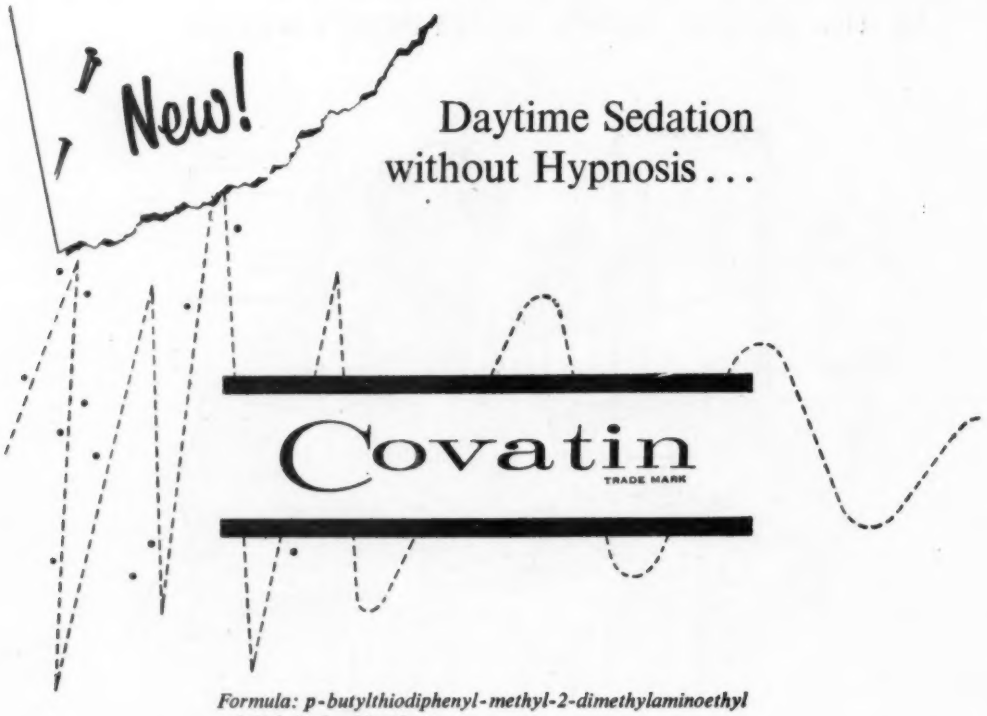

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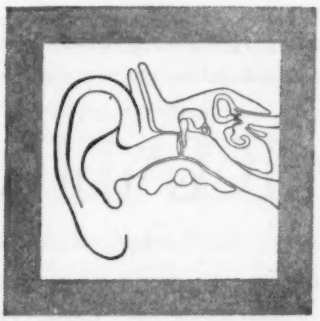

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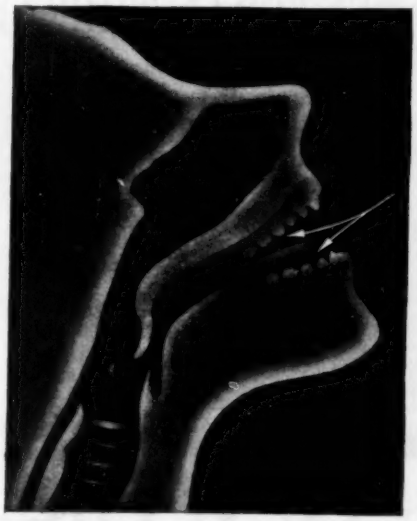

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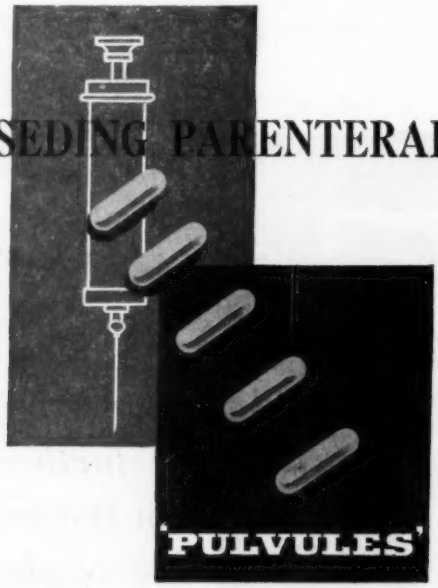

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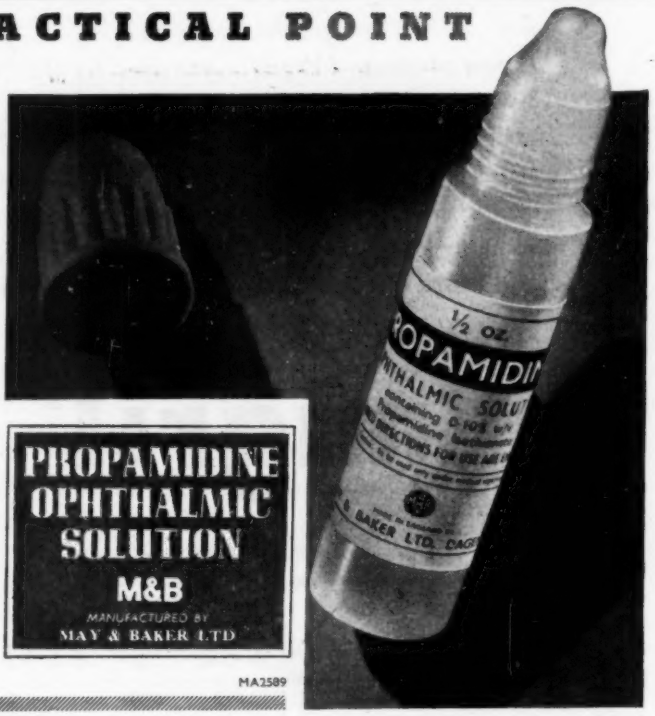

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MITRAL VALVOTOMY
A PROGRESS REPORT

RICHARD W. D. TURNER
O.B.E., M.A., M.D. Camb., F.R.C.P., F.R.C.P.E.
SENIOR LECTURER IN MEDICINE IN THE UNIVERSITY OF EDINBURGH; PHYSICIAN, WESTERN GENERAL HOSPITAL, EDINBURGH

HUGH R. L. FRASER
M.B. Edin., M.R.C.P.E.
ASSISTANT CARDIOLOGIST, STOBHILL HOSPITAL, GLASGOW; LATE SENIOR REGISTRAR, WESTERN GENERAL HOSPITAL, EDINBURGH

THE experience gained from 100 cases of mitral valvotomy has already been reported, together with views on manifestations of rheumatic heart-disease and on the value of special methods of investigation (Logan and Turner 1953).

The first 250 patients from the cardiac department of the Western General Hospital, Edinburgh, have now been analysed, and by discussing results in relation to as many factors as possible, we indicate here how the largest number of patients with mitral stenosis can be benefited by operation with the smallest proportion of disappointments. For this reason we emphasise errors of judgment and causes of disappointing results.

Material

All the patients in this series have been followed up for more than twelve months, 202 for more than two years, 116 for more than three years, 37 for more than four years, and 12 for more than five years. The cases have been analysed in detail in relation to the various factors which may influence the result of the operation.

The series is uniform in that all 250 patients were admitted to the same medical unit and almost all were operated on by the same surgeon (Mr. Andrew Logan). Since all the patients were assessed and followed up by the same team they have been known very well individually. The patients were aged 16–60, 29 being aged 50 or more;

TABLE I—PREOPERATIVE CARDIAC RHYTHM IN 250 PATIENTS SUBMITTED TO MITRAL VALVOTOMY

Age (yr.)	Male	Female	Sinus rhythm	Auricular fibrillation	Total
10–19	2	5	7	0	7
20–29	9	46	47	8 (15%)	55
30–39	16	70	61	25 (30%)	86
40–49	15	58	21	52 (71%)	73
50–60	6	23	6	23 (79%)	29
Total ..	48	202	142	108 (43%)	250

auricular fibrillation was present in 43% (table I), and calcification of the mitral valve in 27% (table V); intracardiac clot was found at operation in 19% (table IV); about a third had aortic incompetence; 12 patients had aortic stenosis, and 6 of these also underwent aortic valvotomy; 5 were pregnant at the time of operation; 24% had considerable cardiac enlargement (cardiothoracic ratio >60%), and many had had congestive failure; 97% had tight (finger-tip) or fairly tight (terminal phalanx) stenosis.

A parallel series of 250 patients were seen over approximately the same period but not advised to undergo surgical treatment.

We deal mainly here with our personal experience, and certain aspects have been discussed in more detail elsewhere—e.g., clinical features of mitral stenosis (Logan and Turner 1953), valvotomy in pregnancy (Logan and Turner 1952a), the diagnosis of mitral incompetence (Logan and Turner 1952b), the diagnosis of aortic stenosis (Logan and Turner 1954), the importance of auricular fibrillation (Fraser and Turner 1955b), and the value of electrocardiography (Fraser and Turner 1955a).

Method

Each patient was assessed in the usual way by history, physical examination, radioscopy, radiography, and electrocardiography. These methods are almost always sufficient for deciding about an operation. Whereas cardiac catheterisation was done as a routine in the first 100 patients, it is now rarely considered necessary unless there is some special indication (see below). Sometimes intra-arterial tracings helped in assessing the severity of aortic stenosis.

Management

Before operation cardiac failure was treated on conventional lines. Unless signs of failure were present, salt was not restricted. Patients with auricular fibrillation were digitalised, but not those in sinus rhythm. In the first 150 cases quinidine was given before operation to all those in sinus rhythm, but this practice was abandoned when it appeared that there was no convincing evidence of its efficacy in preventing postoperative auricular fibrillation. To a few patients with recent embolism anticoagulants were administered preoperatively for three or four weeks, but anticoagulants were not given postoperatively except to the few who developed thrombophlebitis. Valvotomy was done with the finger, with or without the aid of a knife or a mechanical dilator, but we do not discuss surgical techniques here. Penicillin was given to all the patients for ten days. Digitalis was not given after operation to those previously in sinus rhythm unless auricular fibrillation developed. If the fibrillation persisted for fourteen days quinidine was given (see below). All being well, the patients were allowed to get up when they felt like it, usually after the first week. Thereafter a gradual increase in physical activity was encouraged. Ten days after operation they were transferred back to the medical ward. Following discharge from hospital the patients were asked to return for review after a month, three months, six months, and thereafter every twelve months. Some were seen more frequently and a few, living at a distance, less frequently.

Symptoms

Dyspnœa on exertion, paroxysmal dyspnœa, and hæmoptysis are the usual symptoms which bring the patient with mitral stenosis to the doctor. Fatigue is occasionally the primary complaint, but this symptom should always lead to a search for evidence of predominant mitral incompetence, myocardial damage, anæmia, and neurosis. Recurrent hæmoptysis and pulmonary œdema do not necessarily signify tight mitral stenosis, particularly in pregnancy, and may be associated with predominant mitral incompetence. Chest pain and syncope on exertion are more dramatic but much less common manifestations. Systemic embolism or the distress produced by the onset of auricular fibrillation sometimes first bring mitral stenosis to notice.

The symptoms are mainly related to the mechanical effects of mitral stenosis on the lungs. The great variation in pulmonary vascular resistance from medial hypertrophy, intimal proliferation, and (possibly) increase in arteriolar tone, in patients with apparently similar degrees of valvular defect is unexplained. This resistance may tend to protect the lungs from pulmonary œdema but increases the strain on the right ventricle and contributes to eventual cardiac failure. Factors which aggravate symptoms and can partly be influenced by management include exercise—e.g., arduous domestic duties in a woman and unsuitable occupation in a man—auricular fibrillation, pulmonary infection, pulmonary infarction, pregnancy, active carditis, thyrotoxicosis, and anæmia.

TABLE II—GOOD RESULTS IN RELATION TO HEART SIZE AND CARDIAC RHYTHM

Cardiothoracic ratio (%)	No. of cases	Preoperative cardiac rhythm (%)	
		Sinus rhythm	Auricular fibrillation
<50	60	86	67
50–54	55	87	68
55–59	76	84	59
60 or more ..	59	63	47

Breathlessness accompanying normal activities is the principal indication for treatment. Most patients learn to limit their activities short of much discomfort, but on occasion, particularly in young people, discretion is forgotten and we have seen pulmonary œdema precipitated by dancing, by cycling against the wind, and by hurrying in the dark from fear. Emotion may also precipitate pulmonary œdema.

The duration of symptoms in patients with tight mitral stenosis is often surprisingly short, even in the older age-groups. Thus the duration, from the onset of the first symptoms to operation, was two years or less in 25% of the 250 patients and four years or less in 34% of those aged more than 50.

Signs

PALPATION

The value of palpation is confirmed in that it may provide evidence of ventricular hypertrophy which cannot be obtained in any other way, because the radiological assessment of possible ventricular enlargement is often difficult, and the electrocardiogram may be unchanged until hypertrophy is considerable. Right ventricular hypertrophy is an indication for considering operation, and left ventricular hypertrophy is a warning that some important complication is present. A systolic thrill at the apex usually signifies an important degree of mitral incompetence.

AUSCULTATION

Reference will only be made to certain points considered worthy of emphasis.

Sounds.—In mitral stenosis the first heart sound, representing the closure of the valve, is typically sudden, loud, and slapping. More often than not a characteristic additional sound, coinciding with the opening of the mitral valve, can also be heard distinctly. This so-called "opening snap" comes shortly after the second sound and is best heard down the left sternal edge. The presence and qualities of these two sounds are important, but changes in one do not always accompany changes in the other. To an observer familiar with these qualities it is, paradoxically, their absence which is most important in differential diagnosis. In a patient under consideration for mitral valvotomy the absence of either a clear first sound or an opening snap should give rise to concern. Sometimes it will be due to tight stenosis with a rigid or calcmed valve but more often to predominant incompetence. The differentiation of these two extremes, on other grounds, rarely presents difficulty.

Murmurs.—In our experience the duration and other qualities of the mid-diastolic murmur are principally determined by the rigidity or otherwise of the mitral valve and not by the degree of stenosis or pulmonary vascular resistance.

Predominant mitral incompetence.—The auscultatory findings which indicate predominant mitral incompetence are referred to below.

Failure to detect signs of mitral stenosis.—Sometimes, in patients with severe symptoms from tight stenosis and a rigid valve, no abnormal auscultatory signs can be detected when the patient is first seen, but in such cases the characteristic cardiac contour will be apparent on radioscopy. In our experience abnormal signs were always heard subsequently when the patient was re-examined under conditions of different cardiac rate and output.

"*Diaphragmatic valve.*"—It has been claimed that clear signs of mitral stenosis—i.e., a loud slapping first heart sound, an opening snap, and a rumbling diastolic murmur—signify a pliant diaphragmatic valve suitable for valvotomy. In our experience it often happens that operability cannot be predicted on these grounds, and the finding of such a valve at operation is uncommon. When the physical signs are *not* clear, it often happens that a calcified or rigid valve will be found which at best can only be widened to a moderate degree, and even then the functional result may be poor. In some patients with the clearest of signs a most disappointingly rigid valve may be found and little can be achieved despite strenuous efforts with the finger aided by a knife or mechanical dilator, and with such efforts there is always the risk of traumatic mitral incompetence. Very occasionally such clear signs, together with an apical systolic murmur, may even accompany predominant mitral incompetence. On the other hand, in some cases with similar signs surprisingly good splitting of the commissures may be achieved.

TABLE III—INFLUENCE OF AURICULAR FIBRILLATION ON RESULT OF OPERATION

Result of operation	No. of patients with sinus rhythm before operation	No. of patients with auricular fibrillation before operation	Total
Operative death ..	2 (1·5%)	18 (16%)	20 (8%)
Good	119 (85%)	59 (54%)	178 (71%)
Fair	11 (8%)	15 (14%)	26 (10%)
Poor	7	12	19
Subsequent death	1 } 8 (6%)	6 } 18 (16%)	7 } 26 (10%)
Total ..	140	110	250

Special Methods of Investigation

ELECTROCARDIOGRAPHY

Just as absolute reliance can rarely be placed on a single physical sign, so there are few absolute rules about special methods of investigation. Nevertheless

TABLE IV—INTRACARDIAC CLOT

Age			Cardiothoracic ratio			Left atrial enlargement		
Age (yr.)	No. of patients	No. with clot	Ratio (%)	No. of patients	No. with clot	Left atrium	No. of patients	No. with clot
10–19	7	0	<50	60	2 (3%)	+	124	10 (8%)
20–29	55	2 (4%)	50–54	54	4 (7%)	+ +	106	25 (24%)
30–39	86	12 (14%)	55–59	75	15 (20%)	+ + +	15	11 (73%)
40–49	73	22 (30%)	60 or more	61	27 (44%)	+ + + +	5	2 (40%)*
50–60	29	12 (41%)						
Total ..	250	48 (19%)		250	48 (19%)		250	48 (19%)

* 3 cases had associated mitral incompetence.

TABLE V—CALCIFICATION OF MITRAL VALVE

Age (yr.)	Total no. in age-group	Calcification					
		Degree			Sex		Total no. of cases
		+	++	+++	M	F	
10–19	7	2	0	0	2	0	2
20–29	55	2	3	2	2	5	7 (13%)
30–39	86	12	4	8	10	14	24 (28%)
40–49	73	8	7	6	8	13	21 (29%)
50–60	29	2	7	4	5	8	13 (45%)
Total . .	250	26	21	20	27	40	67 (27%)

Calcification occurred in 56% of the males and in 20% of the females.

we consider that the cardiogram may give useful information in the assessment of patients with rheumatic valvular disease, especially in relation to operation. We have analysed our experience in detail (Fraser and Turner 1955a), and for convenience the findings are summarised here.

An entirely normal cardiogram suggests that symptoms may be out of proportion to the real physical disability. If doubt about the necessity for operation exists on other grounds, cardiac catheterisation may give useful guidance.

Left axis-deviation suggests that some significant complication may be present, and other evidence for this should be sought. Tight mitral stenosis may be associated with a normal electrical axis, but the greater the degree of right axis-deviation the more likely is right ventricular hypertrophy (R.V.H.) to be present. In our experience an algebraical sum of R and S in standard lead I amounting to −3 mm. (or less) provides strong presumptive evidence for R.V.H. S>R in V_5, R>Q in a VR, a depth of S in V_5 of 5 mm. or more or a height of R in a VR of 3 mm. or more are other indirect signs providing strong presumptive evidence for R.V.H.

R.V.H. is a strong indication for considering surgical treatment because it usually signifies considerable pulmonary hypertension and a poor prognosis. Tight mitral stenosis is the usual cause, but severe pulmonary hypertension is occasionally asociated with predominant mitral incompetence, and this possibility should be remembered and the other evidence reviewed with care.

Although changes indicating R.V.H. are commonly sought in lead V_1, sole or stronger evidence may be found in V_2 or in the right-side V leads (V_4R, V_5R, VE). An absolute height of R>7 mm. in $V_{1(2)}$ or an R/S>1 in any lead recorded over the right ventricle, irrespective of the absolute height of R, almost certainly signifies R.V.H. Complete or incomplete right bundle-branch block has a similar significance in mitral stenosis; so has a negative T in V_1 if accompanied by a negative T in V_2 or in CR_1. A ventricular activation time >0·03 sec. in V_1 is a sign of R.V.H. but, in our experience, never occurs as a sole sign and is therefore of no practical value. Particular emphasis is laid on the value of the right-side V leads because they give evidence of R.V.H. more often than any other leads and in fact provide the sole evidence in 15–20% of cases. For practical purposes it is sufficient to record V_4R in addition to the conventional chest leads. Depression of the S-T segment may be found when other signs of R.V.H. are well marked. Transient depression may be due to ischæmia. It is important to realise that electrocardiographic signs do not develop until the anatomical degree of R.V.H. is considerable. They were present in 158 (61%) of the 250 patients in the surgical series. It is impossible to grade the severity by the electrocardiogram, because in rheumatic heart-disease various factors in addition to the degree of mitral stenosis and of pulmonary hypertension influence the development of the R.V.H. pattern. Evidence of preoperative progression or postoperative regression of R.V.H. may be recorded.

Finally, there is no absolute electrocardiographic sign of R.V.H., because occasional exceptions have been found or published for every criterion.

Signs of left ventricular hypertrophy (L.V.H.) invariably mean that some important complication is present, and when it is due to mitral incompetence it must be taken as an absolute contra-indication to operation. Likewise signs of biventricular hypertrophy always mean that some important complication is present. When L.V.H. is due to associated aortic valvular disease, severe mitral stenosis may be present in addition, and the relative importance of each defect must be assessed on other grounds.

RADIOLOGY

References will only be made to a few special points because the general value of radiology has been discussed previously (Logan and Turner 1953).

Cardiac Enlargement

The heart's size varies according to general body build and from person to person, even in people of about the same build.

An increase in the transverse diameter of the heart in the postero-anterior view is usually due to right-sided enlargement. The occasional instance in which aneurysmal dilatation of the left atrium forms part of the right border can be readily distinguished. If the left ventricle is enlarged, some cause will usually be evident—e.g., mitral incompetence, aortic valvular disease, and, occasionally, systemic hypertension. Reference is made below to the occasional exception of rheumatic myocarditis. For practical purposes it rarely matters that enlargement of the right atrium cannot always be differentiated from that of the right ventricle.

The cardiothoracic ratio is generally accepted as the best approximate guide to the presence or absence of enlargement and changes in size following treatment, but there are many difficulties as regards the accuracy and validity of serial observations unless changes of considerable degree have taken place. Technical factors are by no means constant in any one radiological department and vary between different departments. Centring varies when judged by eye and not actually measured from the floor to a certain vertebral level. In spite of careful instruction to the patient the breath is not always held in the same phase of respiration. This affects the widest diameter of the chest as customarily recorded and the height of the diaphragm, which in turn modifies the transverse diameter of the heart. The transverse diameter of the heart also depends on whether the exposure is taken in systole or diastole, and serial films may easily be taken in a different phase of the cardiac cycle unless the exposure is timed by an electrocardiograph. For all these reasons caution is required in drawing conclusions from apparent changes in heart size.

Since an analysis of our material shows that the degree of general cardiac and individual chamber enlargement cannot be correlated with the degree or duration of valvular stenosis or incompetence or to the presence or absence of cardiac failure presumably it is principally related to the degree of myocardial damage.

Pulmonary Artery

The apparent size of the pulmonary artery cannot be assessed by the convexity of the arc below the aorta in the anterior view, because this varies in arteries of the same size (measured at operation) and is influenced by the contours immediately above and below. The width of the vessel—i.e., from the mid-sternal line to the outer border—must also be taken into account. A large pulmonary artery is usually associated with considerable pulmonary hypertension, but the converse does not hold. One important factor in the great variations in size which

are seen must be the varying distensibility of the vessel wall.

Peripheral Branches of Pulmonary Artery

We have paid close attention to the narrowing and irregularity in calibre of the peripheral branches of the pulmonary artery which are often seen in patients with severe mitral stenosis, but cannot confirm the practical value of these changes as a measure of pulmonary hypertension. Many variable factors influence the readiness with which these changes are seen; often there is no close correlation between the apparent degree of vascular change and that of pulmonary hypertension, and usually little if any change follows operation. Of more value is the detection of transverse striations.

Transverse Striations

In recent years attention has been paid to the transverse lines best seen in the right costophrenic angle and first described by Kerley (1951). Although by no means pathognomonic of mitral stenosis, in this context they are usually a good guide to the presence of pulmonary œdema in much the same way as a large pulmonary artery and electrocardiographic evidence of right ventricular hypertrophy are good evidence of pulmonary hypertension. In all probability these lines are due to distended lymphatic vessels, and they often disappear after successful valvotomy. They were observed in 37% of the present series. If other factors are favourable, the presence of transverse striations is a strong indication for advising operation.

Left Atrium

If exposure and contrast are good, the postero-anterior film provides a better guide to left atrial enlargement than the customary right oblique position with barium in the œsophagus. In the latter view apparent size depends on the precise degree of rotation and on whether the œsophagus has been displaced to the right or the left by the enlarged left atrium.

We again emphasise that so-called systolic expansion of the left atrium is of no practical value as evidence of mitral incompetence.

Calcification

Valvular calcification is better detected by radioscopy than by either plain radiography or tomography. Its significance as regards the mitral valve is fully discussed below.

Right Atrium

Disproportionate enlargement of the right atrium may be due to disease of the tricuspid valve, in which case the pulmonary artery may be relatively little enlarged, or to myocardial damage. In either case it is a sign of severity of the underlying rheumatic heart-disease.

CARDIAC CATHETERISATION

Our views on the value of cardiac catheterisation are unchanged; in most cases catheterisation is unnecessary because the results rarely influence the decision about operating.

Catheterisation is sometimes of value when the severity of symptoms and signs is in doubt. On the other hand, accompanying the patient up several flights of stairs is a simpler and often an adequate test. There is no convincing evidence that either the shape or the time relationships of the pressure curves, recorded with the tip of the catheter wedged in a peripheral branch of a pulmonary artery, are of reliable practical value in the diagnosis of predominant mitral incompetence. Catheterisation may be of value in the assessment of the respective parts played by aortic stenosis and by mitral stenosis when both defects are present. Severe pulmonary hypertension which increases on exercise can be attributed to the mitral stenosis because there is little pulmonary hypertension from diseases of the aortic valve unless left ventricular failure is present. On the other hand, if one is reasonably certain that the degree of aortic stenosis is important—e.g., from electrocardiographic evidence of left ventricular hypertrophy—other special investigations are unnecessary because mitral and aortic valvotomy can be done at the same thoracotomy. Catheterisation is also of value when the relative parts played by chronic bronchitis and emphysema and by mitral stenosis are in doubt.

It has been claimed (Harvey et al. 1955) that, in a patient believed to have severe mitral stenosis, failure of the pulmonary arterial pressure to rise on exercise can be accepted as presumptive evidence that myocarditis is the limiting factor, and this fits in with our own observations.

Operative Risk

Of these 250 consecutive patients 16 died during the operation, or shortly afterwards, giving an immediate mortality of 6·4%, but 4 other patients died within two months, while still in hospital, from conditions that must be attributed to the operation, making the over-all operative mortality, from the commencement of the series, 8%. However, the operative risk for an individual patient cannot reasonably be assessed from the analysis of a large series such as this, which consists of patients of differing age with various degrees of severity judged by cardiac enlargement, cardiac failure, and cardiac rhythm, and various degrees of associated mitral incompetence, aortic valvular disease, pulmonary disease, and systemic hypertension.

In a patient aged less than 40 with the signs of uncomplicated mitral stenosis, sinus rhythm, no more than moderate cardiac enlargement, and no history of cardiac failure or of systemic embolism the risk is small and no more than that of the occasional mishap which accompanies almost any surgical operation or anæsthesia. No such patient died in this series. On the other hand, in a patient aged more than 50 with considerable enlargement, auricular fibrillation, and a history of systemic embolism or of gross cardiac failure the risk may be as high as 20%, mainly from embolism or from cardiac arrest at the operation. In our experience, if there has been a history of systemic embolism, the chances of clot being present in the auricle or the atrium are high; and, if clot is present, there is a 20% risk of systemic embolism at the operation.

The over-all mortality in patients with a cardiothoracic ratio under 60% was 5%. In patients aged less than 50, even with moderate cardiac enlargement and auricular fibrillation but without any history of systemic embolism, the operative mortality was 3%. In the last 100 cases there were 3 deaths.

From the analysis of our material we appreciate that, with a stricter selection of cases, some deaths might have been avoided, and in this respect there must be regrets. Nevertheless, although very few deaths will take place if only "good risks" are accepted, such a restricted selection would deny a new lease of life to many patients with a considerable or severe disability (see below). The deaths due to the operation were as follows:

	Cause	*No. of deaths*
Early (16):	Cerebral embolism	6
	Cardiac arrest	3
	Hæmorrhage	2
	Hepatic failure	2
	Hypotension	1
	Intracardiac thrombosis	1
	Transfusion reaction	1
Late (4):	Mitral incompetence	3
	Cerebral embolism	1
	Total	20

Early Operative Deaths

The principal causes of death during or shortly after operation were cerebral embolism from the displace-

ment of intra-auricular or intra-atrial clot or of fragments of calcified mitral valve; and cardiac arrest or ventricular fibrillation. In addition 2 patients died from hæmorrhage secondary to technical difficulties, 2 from hepatic failure secondary to cardiac cirrhosis of the liver, 1 from a mismatched blood-transfusion, 1 from cardiac failure three days after operation, apparently as a result of the postoperative formation of clot occluding the mitral valve, and 1 from persistent hypotension.

Of the 3 patients with cardiac arrest or ventricular fibrillation, the first was a woman, aged 51, with a very large heart, a heavily calcified valve, and an intra-atrial clot; the second was a woman, aged 58, with considerable cardiac enlargement; and the third was a woman, aged 38, with a very large heart and aneurysmal dilatation of the left atrium. In each instance it was considered that the operative risk was above average owing to the degree of cardiac enlargement, which presumably indicated muscle damage, and such patients should probably not be subjected to operation.

From experience of this series and of other patients with severe cardiac cirrhosis of the liver subjected to operation under general anæsthesia we have decided that the risk of hepatic failure in such cases is prohibitive.

Later Operative Deaths

2 patients died, four and eight weeks after operation, with cardiac failure which was probably secondary to traumatic mitral incompetence. A regurgitant jet and an apical systolic murmur followed valvotomy, but the the degree of mitral incompetence produced was difficult to assess post mortem. In a 3rd patient, who died eight weeks after operation, traumatic mitral incompetence was definitely the cause. The 4th death was in a woman, aged 59, who developed paroxysmal auricular fibrillation during the night, at home, eight weeks after operation. Three days later she had a fatal cerebral embolism, presumably as a result of thrombosis during the period of rapid ventricular action.

Subsequent Deaths

7 patients died from one to thirty-nine months after leaving hospital; 1 death was probably attributable to quinidine; 1 was due to an unrelated pulmonary condition; 1, who discharged herself against advice, may have died from bacterial endocarditis; in 1 young girl the operation appeared to be only an incident in her progressive deterioration due to active carditis; 1 woman died suddenly three months after successful valvotomy and no cause was apparent at necropsy; and 2 patients with gross cardiac enlargement, of a degree which we now consider precludes operation, had a poor symptomatic result and died from the natural consequences of mitral stenosis two years and three and a quarter years after operation.

Results in Survivors

Grading (Subjective)

By a good result we mean freedom from congestive cardiac failure, attacks of pulmonary œdema, and hæmoptysis, and a striking improvement in effort dyspnœa. By a fair result we mean that both patient and doctor are convinced that the operation was well worth while in that a material degree of symptomatic improvement was obtained. By a poor result we mean that the condition did not improve or became worse after the operation.

Subjective Assessment

Subjective evidence of improvement is difficult to assess. It is simple enough to decide whether the patient considers the operation to have been worth while (almost all do so at least for a time); but whether a result is to be classified as fair, good, or very good depends on numerous variable factors, including the length of follow-up.

In the first place the degree of previous disability varies widely. Young people expect to be able to do more than older ones; some tolerate their symptoms better than others. If symptoms were progressive, some patients were operated on when the condition was mild to prevent further deterioration and destruction of the valve; whereas others, who found life almost intolerable, were anxious to be treated if no more than a fair chance of improvement could be offered. Most were principally disabled by dyspnœa on exertion, but in some the chief indication for operation was recurrent hæmoptysis, systemic embolism, attacks of pulmonary œdema, or, occasionally, angina. A few patients who improved considerably at first and continued to do so for two or even three years have recently shown evidence of regression. 5 have been subjected to a second operation owing to an inadequate first valvotomy when experience was limited.

Objective Assessment

Objective evidence of improvement is not easy to obtain; the least equivocal is provided by the electrocardiogram.

In our experience the *auscultatory signs* of mitral stenosis are rarely materially altered by operation, and this is not surprising, because only the degree of stenosis and not the quality of the valve cusps is changed by the operation. In no case did the auscultatory evidence for mitral stenosis completely disappear.

The *nutrition* often improves.

On *radiography* the heart size, judged by the cardiothoracic ratio, may be reduced, but there are considerable difficulties in assessing it (see above). The transverse striations mentioned above often disappear.

Electrocardiography may show regression of the pattern of right ventricular hypertrophy. 14 (9%) of 158 patients with signs of R.V.H. died, and in 10 (6%) who live at a distance, although clinical rpports have been received, adequate follow-up electrocardiograms are not available. The electrocardiographic signs of R.V.H. disappeared in 26 (16·5%), regressed variably in 38 (24%), and are essentially unchanged in 70 (44%). Many patients in whom there has been no electrocardiographic change have had an excellent symptomatic result, but in this group well-developed patterns of R.V.H. had not been present, the signs being inconspicuous in the majority.

Few of our patients were subjected to *re-catheterisation*. Initially some volunteers were re-examined in this way because we wished to study the natural history of the condition after operation. However, it became clear that serial observations would have to be made because improvement often progressed over many months and because some conditions during the catheterisation—e.g., the degree of relaxation of the patient and the amount of exercise given—could not be precisely reproduced, and therefore errors of deduction might be considerable. Some patients, however, were re-catheterised to assess the degree of pulmonary hypertension before deciding on reoperation.

Analysis of Poor Results

Systemic Embolism

2 survivors sustained hemiplegia from displacement of calcified material, and made a moderate functional recovery.

Poor Selection of Cases

Cardiac enlargement depends mainly not on the degree or duration of valvular defects but presumably on the degree of rheumatic myocardial damage. A good result was obtained in only 51% of patients with a cardiothoracic ratio >60% but in 82% of those with a ratio <55%. The combination of a large heart, auricular fibrillation, and the absence of electrocardiographic

signs of right ventricular hypertrophy is particularly unfavourable.

Associated mitral incompetence in 8 patients was less severe than had been predicted; consequently it was only to be expected that there would be no dramatic improvement in symptoms as a result of the modest degree of splitting of the commissures that was achieved. In occasional cases of special difficulty exploratory thoracotomy is justifiable; but, if due attention is paid to all the relevant signs, errors of judgment on this account should now be rare.

Active carditis.—On the whole there has been a poor correlation between the histological findings in the biopsy specimen taken from the left auricle at operation (250 cases), the erythrocyte-sedimentation rate, and clinical and electrocardiographic evidence of active carditis. However, in a few patients active carditis is believed to have been the reason for an unsatisfactory result despite adequate valvotomy.

Pulmonary disease.—In 4 patients chronic bronchitis is still troublesome, but each considers the operation to have been worth while.

Inadequate Valvotomy

In 4 patients without calcification a poor result was attributed to inadequate splitting of the commissures because of rigidity of the valve. No other adverse factor appeared to be responsible. In 4 patients gross calcification of the mitral valve may have been responsible for a poor functional result despite good splitting of the commissures, but 2 of these patients also had very large hearts.

Traumatic Mitral Incompetence

In 6 patients it is believed that a material degree of mitral incompetence produced as a result of mitral valvotomy contributed to a disappointing result; 3 of these patients are included in the deaths. There is no doubt that, in patients with a rigid valve, when vigorous attempts are required to achieve adequate splitting of the commissures either with the finger, a knife, or a mechanical dilator, a higher incidence of traumatic mitral incompetence will result. However, there is also no doubt that in other patients such efforts have produced better results than were obtained earlier in our experience.

Postoperative Complications

Cardiac Failure

Postoperative retention of fluid, shown by a rise of venous pressure and slight peripheral œdema, is very common in the first postoperative week but, unless persistent, does not require treatment with mercurial diuretics or with digitalis. Frank congestive failure is very uncommon.

Auricular Fibrillation

Postoperative auricular fibrillation in those previously in sinus rhythm developed in 24% of the patients. In most instances fibrillation develops in the first few postoperative days, but occasionally the onset is delayed for a week or two and then is possibly related to increasing physical activity. Occasionally the onset was apparently precipitated by some minor surgical procedure—e.g., bronchoscopy and paracentesis thoracis—but usually there was no obvious reason. It is presumed that fibrillation in these patients is related to traumatic pericarditis and epicarditis in the setting of rheumatic heart-disease. We found it was impossible materially to decrease the incidence of postoperative fibrillation by the administration of quinidine prophylactically even in fairly high dosage, such as gr. 24–36 daily. We also found, as have others, that it was unprofitable to attempt to restore sinus rhythm by treatment with quinidine in the first ten postoperative days, because success was uncommon. However, when quinidine was given after the first fortnight, sinus rhythm was restored in all but 2 cases. We have been unable to demonstrate that digitalis given before operation has any effect in diminishing the occurrence of postoperative auricular fibrillation.

Postoperative Pyrexial Syndrome

Since pyrexia and some pain in the chest are very common in the first week or ten days after operation and usually subside by the time the patient should be up and about, we take no particular note of them. Occasionally, however, they persist longer or develop some weeks after operation and are accompanied by pains in the joints, and very occasionally they recur during subsequent weeks. Sometimes the chest pain is severe. Signs of cardiac failure (increased venous pressure and peripheral œdema) are common in the early postoperative period and may be somewhat accentuated in patients who develop this pyrexial syndrome but they subsequently subsided in all the cases. Although this complication superficially resembles rheumatic fever, we are not convinced that this is the cause, because in our experience there has been no joint swelling, little subjective improvement with salicylates, and, after subsidence of the attack, no evidence of deterioration in the cardiac condition. The course is uninfluenced by antibiotics. The syndrome is probably due to traumatic pericarditis and pleuritis resulting from the operation, with accompanying systemic disturbances. Some workers report an incidence of this syndrome in 25–40% cases. In our series it was less than 5%. It is important that this syndrome should be widely recognised because, when it occurs later—i.e., after the patient has returned home—it may lead to admission to a local hospital and give rise to unnecessary alarm.

Personality Change

We have observed personality change and occasionally frank psychoses, as have other workers. All the patients recovered.

Subsequent Progress

Deterioration after Initial Improvement

If postoperative grading is accepted as established six months after valvotomy, 22 patients are to be considered as regards subsequent deterioration. If 5 patients subjected to a second valvotomy because of an inadequate first attempt and 4 who developed non-cardiac complications (such as cancer) are excluded, 13 remain who did not maintain their initial improvement. The initial results had been fair in 6 and poor in 1; so only 6 of our 250 patients operated on more than a year ago, in whom adequate valvotomy was achieved and the initial result was good, deteriorated. Valvotomy is in no sense a cure, and it is only to be expected that the number of patients who maintain a good initial result will decrease progressively; but, so far as the first few years are concerned, it seems that the result is usually determined by the surgeon at the operation.

In most cases the subsequent course has been essentially the unfolding of the natural history of mitral stenosis in advanced cases, and in 4 of these the development of auricular fibrillation was apparently responsible for the onset of deterioration. In 1 patient retinal embolism was the reason for dropping a grade.

Re-fusion of Commissures

The possibility of re-fusion must be entertained whenever symptoms recur after valvotomy. Such an occurrence must, of course, be distinguished from mere progression of symptoms in the natural course of mitral stenosis when, for one reason or another, the operation was unsatisfactory. Symptoms, however, sometimes recur after a considerable period of unquestionable improvement.

In our experience re-fusion of the commissures must be very uncommon. 5 of our patients were subjected to a second valvotomy, and 3 more are under considera-

tion, but in each case the first operation was early in our experience. 7 of these 8 patients were among the first 15 to be treated, and the 8th was no. 53. The reason for the recurrence of symptoms is difficult to demonstrate conclusively, but the second valvotomy was done by the same surgeon, and in his opinion inadequate splitting of the adherent commissures at the first operation rather than re-fusion was the condition found. If this is the case, myocardial failure from inadequate valvotomy is presumably responsible for subsequent deterioration. In each of the 5 patients the second operation produced much improvement, which so far has been maintained (twelve months to three years).

That re-fusion is likely to recur often seems improbable on theoretical grounds because the surfaces of the valve leaflets usually consist of avascular fibrous tissue which would not be affected by a recurrence of active carditis. However, with adequate splitting and little resultant improvement in cusp movement there must be a possibility of thrombosis in the narrow slit-like aperture between the partially divided commissures.

That re-fusion can take place is well illustrated by a case of Blalock's (McKusick 1955) and a case described by Matthews (1954). However, from the published reports it seems that most of the cases described can be better explained on the basis of inadequate valvotomy.

In the last 200 cases of the present series there was no reason to suspect re-fusion, and from the practical point of view this possibility is not at present important and should not influence the decision about operating.

Factors Influencing Result of Operation

Age over 50

Of the 250 patients 29 were aged 50 or more, 8 being over 55 and the eldest 60. 7 died as a direct result of the operation; 2 from cardiac arrest, 4 from cerebral embolism, and 1 from traumatic mitral incompetence. 2 of those with cerebral embolism died in the early days before the importance of allowing gushes of blood to escape from the auricle before valvotomy was appreciated. Of these 29 patients 80% had auricular fibrillation and about 50% each had clot, calcified valves, or a cardiothoracic ratio of 60% or more; 1 of them has since died. In 20 survivors treated more than twelve months ago 13 results are good, 4 are fair, and 3 are poor —i.e., worth-while improvement was obtained in 65%. As in analysing the importance of auricular fibrillation as opposed to sinus rhythm, it is impossible to assess the effect of age because of the other variable factors involved, such as cardiac size, calcification, and clot; but it is clear that the operative risk is greater than in the younger age-group and good results are less likely to be obtained. However, a good result was obtained in 7 of 8 patients with a cardiothoracic ratio less than 60% who had no past history of embolism. The 8th patient, aged 59, died at home as a result of an attack of uncontrolled paroxysmal fibrillation, which is an uncommon event.

Cardiac Enlargement

On the whole the larger the heart the poorer is the outlook because, as mentioned above, cardiac enlargement reflects not so much the degree or duration of mechanical valvular defects as the degree of myocardial damage. Hypertrophy judged electrocardiographically, without much cardiac enlargement judged radiologically, is at least partly reversible, but the effects of rheumatic myocarditis are not. In our experience a reduction in over-all cardiac size has been uncommon after successful valvotomy.

In this series enlargement judged by the cardiothoracic ratio was divided into four grades: <50%, 50–54%, 55–59%, and 60% or more. The results in the fourth grade, as might be expected, are definitely less good than in the grades with less cardiac enlargement (table II). Nevertheless considerable enlargement is not an absolute contra-indication to operation.

Gross enlargement of the left atrium is not necessarily a sign of predominant mitral incompetence and may occur with tight stenosis; and gross enlargement of the right atrium is not necessarily a sign of tricuspid disease or of severe pulmonary hypertension. Good operative results are unlikely to last in either of these groups. Enlargement of the left ventricle, where not attributable to aortic valvular disease, is almost always due to mitral incompetence but occasionally may be found with tight mitral stenosis, presumably as a result of rheumatic myocarditis.

Finally, severe mitral stenosis may occur rarely in the absence of any enlargement of the right atrium or ventricle, with but slight enlargement of the left atrium and with normal lung fields.

Auricular Fibrillation

In the surgical series 111 of 250 (44%) patients had auricular fibrillation before operation, and 34 of 140 (24%) of those previously in sinus rhythm developed fibrillation in the early postoperative period. Only 5 patients developed fibrillation later than that.

In the medical series 115 patients were considered unsuitable for operation because the mitral stenosis was too mild, and 135 because it was too severe or because of some other factor complicating mitral stenosis—e.g., mitral incompetence or aortic valvular disease. Of the mild group 5 (4%) had auricular fibrillation, and of the severe group 110 (81%).

Precipitating factors which we have observed include exertion, emotion, infection, active carditis, and thoracotomy, but usually there is no obvious cause.

Clinical aspects of auricular fibrillation in rheumatic heart-disease have been discussed elsewhere (Fraser and Turner 1955b); here fibrillation will be considered only in relation to operation and its results. From this point of view disadvantages are from the greatly increased probability that clot is present in the auricle or in the atrium, with the consequent risk of embolism at operation, and from the presumed presence of myocardial damage, which probably explains why postoperative improvement, though often striking, is more often less so than in patients with sinus rhythm. This is only to be expected because, before the introduction of valvotomy, the onset of auricular fibrillation in a patient with mitral stenosis reduced the probability of survival to no more than a few years. Oleson (1955) found that 50% of patients lived for less than six years. Prognosis cannot be directly related to the effects of fibrillation per se, because other related factors, such as the presence of clot, and unrelated factors, such as calcification of the mitral valve, influence the operative result.

The results obtained in those with auricular fibrillation who had comparable degrees of cardiac enlargement judged by the cardiothoracic ratio are shown in table II.

Sometimes the importance of auricular fibrillation has been underestimated (table III). All but 2 of the operative deaths took place in patients with auricular fibrillation; and, except for 1 patient with an unrelated pulmonary condition, all the subsequent deaths took place in patients with fibrillation. Also twice as many of the results classified as poor or fair were in those with fibrillation as in those with sinus rhythm, and 81% of those considered unsuitable for surgical treatment on grounds of severity had auricular fibrillation.

Conclusion

Auricular fibrillation is not a contra-indication to operation but is a relative disadvantage in that the incidence of clot and therefore the risk of systemic embolism are much greater than in patients with sinus rhythm and there is less chance of a good result.

(*To be concluded*)

OUTCOME OF SURGERY FOR ULCERATIVE COLITIS

B. N. BROOKE
M.D. Birm., M.Chir. Camb., F.R.C.S.
READER IN SURGERY, UNIVERSITY OF BIRMINGHAM

"WHAT is the expectation of life of patients who have had total colectomy for ulcerative colitis ? Do they make 'old bones' ? " This paper is presented in answer to these questions posed by Gabriel (1953). To the end of 1955, 131 patients with ulcerative colitis had come under my care for operation ; for 5 patients only emergency or diagnostic laparotomy was undertaken ; 126 underwent elective surgery. All cases of "right-sided colitis" (syn. entero-colitis) have been excluded on grounds that have been discussed elsewhere (Brooke 1954, Cooke and Brooke 1955).

Sex, Age, and Duration of Disease

There were 84 females and 47 males—a ratio of almost 2 : 1. Fig. 1 shows the age-distribution at the time of the first operation, together with the duration of the disease before the first operation. In my experience the disease is less common in the first two decades of life. The youngest patient was operated on (ileoproctostomy) at the age of 6 years, the disease having started two years earlier. The youngest age at which I have encountered the condition is 2 years, but surgery has so far been avoided in this girl.*

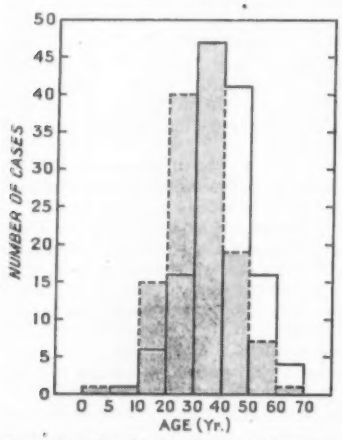

Fig. 1—Age-distribution at onset of disease (interrupted line) and at time of first operation (continuous line).

Indications for Surgery

Surgery was undertaken when the patient's general condition had continued to deteriorate, despite conservative measures ; when a patient was otherwise unlikely to return to normal life ; for complications, both ano-rectal and remote ; for the acute emergencies of hæmorrhage and perforation ; for carcinoma, or to remove this potential hazard in late cases. Fig. 2 shows that, when undertaken on these grounds operation is commonly done either early in the disease, or after ten years. In only a few of the late group was the possibility or the presence of cancer the prime indication.

Ætiology

On the assumption that ulcerative colitis is caused by antecedent trauma to the colon (Brooke 1953, 1954), or by failure of normal regeneration of epithelium, aggravated by extrinsic factors (Lumb and Protheroe 1955), it is possible that precipitating factors may be revealed in the history.

7 patients had a history of dysentery (Hurst and Knott 1936, Felsen 1945, Stewart 1950, Dowdell et al. 1953), with amœbic infestation in 3. 1 patient had had respiratory symptoms of an allergic nature with pronounced eosinophilia (Andresen 1953) ; in another, bowel symptoms had persisted from a period of purgation (Sloan et al. 1950). These factors were not appreciated when this series began, so that significant points may have been overlooked when eliciting earlier case-histories. The numbers therefore cannot be regarded as absolute.

Stress, in its psychological sense, was observed in many, but only in relation to the humiliation and general sense of ill-being arising from continued and severe diarrhœa. Signs of stress disappeared after the elimination of diarrhœa. To an eye untutored in the refinements of psychiatry there appears to have been no clear example of stress from other causes. There was evidence of familial incidence (Felsen and Wolarsky 1955) in only 1 patient, whose brother also has colitis.

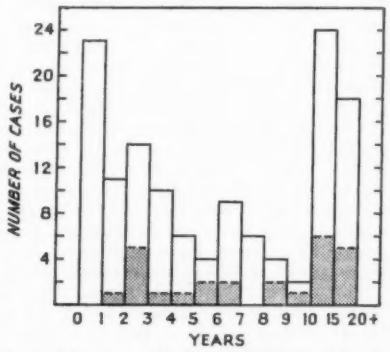

Fig. 2—Histogram showing the duration of disease at time of first operation in whole group (continuous line), and in patients with colo-ileitis (interrupted line).

Surgical Treatment

The routine programme for curative treatment has been excision of the large bowel with institution of a permanent ileostomy. At first this was undertaken in three stages—ileostomy, colectomy, and excision of rectum. It is now done in one stage (primary panproctocolectomy) or, if the patient's condition will not permit a dissection in the pelvis, in two stages (primary colectomy and rectal excision, or ileostomy and panproctocolectomy). 117 patients were submitted to this elective routine (table I). Their condition at the time of operation varied from moribund—owing to perforation or severe electrolyte and protein depletion—to fair ; but the majority were seriously ill.

Preservation of Anal Sphincters

Resection and anastomosis with preservation of anal function was undertaken in 9 patients for the following reasons : in children to gain time until an age is reached when the ileostomy can be managed (1 case) ; in the rare patient whose rectum is not seriously damaged (4 cases) ; in those with a limited area of bowel involved (2 cases) ; in patients with mental deficiency or deterioration to a degree which would make ileostomy management difficult (2 cases). Simple resection and end-to-end ileorectal or ileosigmoid anastomosis was performed in one stage in all except 2 patients, who required only a

TABLE I—ELECTIVE SURGERY IN 126 PATIENTS

Operation	No.	Deaths
Ileostomy*	42	2
Colectomy	23	2
Panproctocolectomy	19	..
Primary colectomy	49	3
Primary panproctocolectomy	15	2
Excision of rectum :		
Perineal	9	..
Abdominoperineal	55	1
Resection and anastomosis †	9	1
Total	221	11

* 1 patient in the ileostomy group also had a partial gastrectomy.
† 3 patients in the resection and anastomosis group had subsequent conversion to a permanent ileostomy.

* Resection and anastomosis has since been performed.

limited resection for disease which appeared to be localised following a previous cæcostomy or appendicostomy. In 3 of these 9 patients it later became necessary to unpick the anastomosis and institute a permanent ileostomy. Of the 117 patients submitted to permanent ileostomy when first seen by me, 1 had previously had an ileorectal anastomosis elsewhere. In this case excision of the rectum became necessary because of the onset of arthritis; and, until the time her rectum was removed, she had endured a permanent fæcal fistula from the anastomosis.

Operative Mortality

Operative mortality in my hands has been 5%, though the total operative mortality of this group of patients is slightly lower, since twenty-one operations had previously been performed elsewhere on 18 patients—eleven ileostomies, four colectomies, three cæcostomies, one appendicostomy, one colostomy, and one resection. In 1 patient gastric ulcer, causing an hourglass deformity of the stomach, necessitated partial gastrectomy as well as ileostomy. This patient did well and panproctocolectomy has since been performed. Table II shows that at least 6 deaths were due to avoidable failures of technique; reduction in mortality should therefore be possible.

The first operation is the most dangerous, 8 of the 11 deaths resulting from the initial procedure. The patient-operative mortality was 9%; to this must be added 4 deaths during follow-up—1 from lung abscess, 2 from obstruction, and 1 from carcinoma. With a total of 15 deaths the over-all mortality of the condition treated by surgery was 12%. The 129 patients studied by Rice-Oxley and Truelove[6] (1950) provide a group for comparison since they were admitted to hospital and treated conservatively. The mortality in this group was 22% during the first year of the disease, rising to 31% after five years. The comparison cannot be strict, however, since in my series there is a lower proportion of patients during the first attack of the disease, when more deaths may be expected. To offset this, it may be presumed that there is a greater selection of more severe cases in a group which is entirely surgical than one which was primarily medical (only 16 of Rice-Oxley and Truelove's patients were operated upon).

TABLE II—CAUSES OF 11 OPERATIVE DEATHS

Operation	No.	Cause
Ileostomy	2	Obstruction in para-ileal gutter Persistent electrolyte imbalance with preop. and postop. tetany
Colectomy	2	Hepatorenal failure Subcutaneous wound dehiscence and obstruction of small-bowel loop
Primary colectomy	3	Pelvic abscess Electrolyte imbalance and obstruction at ileostomy Pneumonia; death on the table
Primary panproctocolectomy	2	Infection in posterior abdominal wall at site of pyonephrosis previously treated by nephrectomy Pneumonia
Abdominoperineal excision	1	Small-bowel fistula following operative trauma
Resection	1	Fistula at site of anastomosis

The introduction of cortisone and corticotrophin in the treatment of ulcerative colitis may prove to have reduced the death-rate in cases treated conservatively. Neither drug was used in my series as a preparation for surgery, though some patients had been included in the cortisone trial (Truelove and Witts 1955), while others, outside that investigation, had received cortisone. Cortisone was gradually withdrawn before operation, but this was not always possible since patients failing to respond to the drug were usually those most seriously ill and requiring operation urgently.

Fig. 3—Incompetent ileocæcal valve leading to secondary ileitis.

After excluding those who died 67 patients submitted to the ileostomy routine have now reached the third year or more since ileostomy was instituted; and in 39 of these five years or longer have elapsed since the first operation. Of those submitted to resection and anastomosis 3 have reached the third year since operation.

Complications of the Disease

Local Complications

Colo-ileitis.—This results secondarily from reflux through the ileocæcal valve which is so damaged by the disease as to become incompetent (Brooke 1953, 1954) (fig. 3); and to differentiate this condition from the ileitis associated with enterocolitis, colo-ileitis is the most suitable designation. The length of ileum involved is usually limited to one to two feet, and the involvement is never sufficiently serious to impair small-bowel function. Steatorrhœa was not seen in any of the 15 cases in this series proved by examination of operation specimens. The valve was incompetent in all of them, and in another 11 patients in whom ileitis had not yet developed. No patient was seen with ileitis and a normal valve.

This extension of the disease into the ileum is not specifically a feature of long-standing disease, as a comparison between the duration of the disease in these 26 patients and the whole group reveals (fig. 2). Rather does the condition reflect the totality of large-bowel involvement in certain patients, for the valve is never incompetent unless the cæcum and ascending colon are ulcerated. It has been my experience that ileitis may be suspected in those patients who are most emaciated (fig. 4); yet none of these patients died following the initial operation—primary colectomy in 14 and primary panproctocolectomy in 1. After the institution of an ileostomy, the ileal condition subsided even when inflamed ileum was used for the construction of the ileostomy—this is in sharp contrast to patients' progress after ileostomy performed for enterocolitis (Cooke and Brooke 1955). It is therefore unnecessary to sacrifice small bowel in cases of colo-ileitis in an endeavour to construct the ileostomy from normal intestine. Furthermore, ileitis, judged by clinical behaviour and the

appearance of an ileostomy, has not recurred in 14 patients, 7 of whom have reached the third year or more since operation. In 1 case of late death (from obstruction with multiple adhesions) ileitis was found at necropsy, but this was possibly associated with the obstruction.

Ileitis developed in 1 further patient who required conversion of an ileorectal anastomosis to permanent ileostomy, and in whom the condition did not exist before the anastomosis.

Anorectal lesions.—Fissure was the most common anal complication. It often represented an extension of rectal ulceration across the anorectal ring, when incontinence was usual. Fistulæ and ischiorectal abscesses were present in 36 patients, in 15 of whom rectovaginal or rectovulval communications were present (19% of all women); and in 1 man a fistula was present either into the bulb of the urethra or just above this level through the prostate. Stricture had formed in the rectum or anal canal in 17 patients, 1 of whom also had a stricture in the ascending colon which proved to be carcinomatous (fig. 5). In 2 further patients strictures were found in the transverse colon. 1 rectal stricture was also the site of a carcinoma.

Carcinoma.—This has been encountered in 3 women and 1 man.

In the man the condition was inoperable: he was one of the 5 cases submitted to laparotomy alone; and he lived for two and a half years after laparotomy. The condition was recognisable clinically in a woman who at the age of 55 had had ulcerative colitis for twenty-four years; she died of metastases a year after primary panproctocolectomy. In the other 2 patients the diagnosis was only ascertained by histological section taken from areas of stricture: 1 case has already been mentioned (fig. 5); in the other, biopsy of a stricture which had formed above a rectovaginal fistula led to the diagnosis. In neither was the lesion evident on naked-eye inspection of the bowel. Both survive following panproctocolectomy, 1 after three years and the other after five.

It therefore seems that the prognosis with carcinomatous degeneration may not be hopeless, provided the condition is recognised and the lesion excised at an early stage. With 4 out of 131 cases, the incidence of carcinoma in the total group is 3%. But all 4 patients had suffered from ulcerative colitis for ten years or more; and the incidence

A B

Fig. 4—Patient whose bowel is shown in fig. 3: A, at time of primary colectomy; B, two and a half years later.

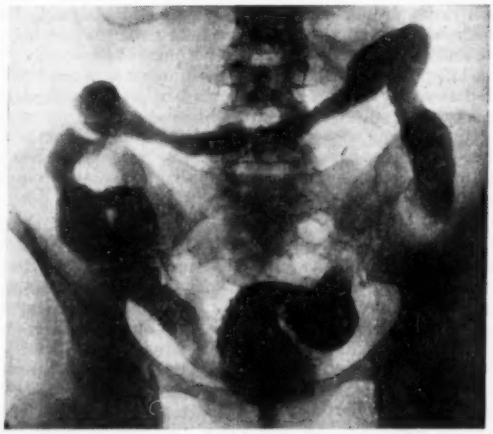

Fig. 5—Barium enema showing stricture below hepatic flexure. This led to colectomy on suspicion of malignancy, which was proved histologically but was not evident to naked eye.

of carcinoma in those with a history of ten years or longer in this series (42 patients) rises to 10% (Cattell 1948, Counsell and Dukes 1952).

Perforation.—Gross colonic dilatation is a useful sign of impending perforation (Brooke 1954, Lumb and Protheroe 1955); and this catastrophe can sometimes be avoided by timely colectomy. (Dilatation is not, however, always the prelude to perforation.) Perforation is easily missed, since the classical signs associated with perforation of a hollow viscus into the peritoneal cavity are frequently absent—as they were in the 6 cases of this series.

Laparotomy was performed in desperation on 1 patient who was moribund four days after perforation. Elective surgery could not be undertaken on this patient, nor on another whose colon was found at laparotomy to have so disintegrated after six weeks' treatment with cortisone that the colonic wall was replaced by the abdominal parietes in the descending and sigmoid areas. Both these patients died.

The 3rd patient was operated on within twelve hours of perforation. Primary colectomy was performed and he survived—even though it subsequently transpired that the site of perforation was in the upper rectum and had not been removed.

In the 4th patient perforation took place after primary colectomy in the lower sigmoid area, distal to the excision. This led to a subphrenic abscess, and a persistent fistula which was cured by abdominoperineal excision of the remaining large bowel.

In the remaining 2 cases perforation had not led to peritoneal contamination but was discovered, at routine colectomy, on the posterior surface of the ascending colon in 1 patient (where a pericolic abscess had developed as a result) and at the splenic flexure in the other (where it had become encompassed by omentum and spleen).

Hæmorrhage.—This was a predominant feature, leading to severe anæmia, in 4 patients.

2 of them were treated successfully by primary colectomy and 1 by primary panproctocolectomy. The 4th patient, a girl aged 15, required emergency primary colectomy for repeated exsanguinating hæmorrhage. Severe bleeding then persisted from the rectum and—though instillations of snake venom and adrenaline brought some measure of control—abdominoperineal excision had to be undertaken ten days later.

All these patients survived.

Fulminating disease.—This beggars exact definition. If the term is reserved for patients with severe toxæmia, pyrexia to 103–104°F, lethargy verging on coma, and serious alteration of blood chemistry, it was present in

13 patients. 7 were treated by primary colectomy with 2 deaths, and 6 by ileostomy with 1 death.

In some patients—as in all 3 who died—the blood chemistry was so disarranged (figures as low as serum-protein 4 g. per 100 ml. and serum-potassium 2·9 m.eq. per litre encountered), with diarrhœa so persistent, as to defy all attempts at correction. By the time blood changes have become irreversible it appears that surgery is unlikely to be successful. Primary colectomy, rather than ileostomy, is often advised for the fulminating disease on the logical ground that toxic absorption, together with fluid, protein, and electrolyte loss, is thereby immediately reduced. At the Lahey clinic, however, ileostomy has been the initial operation of choice (Cattell 1953). Though I prefer to undertake primary colectomy if possible, there are occasions when ileostomy alone is all that a patient can sustain.

In my experience ileostomy has no greater mortality than primary colectomy, though convalescence is slower after ileostomy alone.

Remote Complications

Arthritis.—This was the commonest remote complication (17 patients, 13%). It affected the large joints—especially the knee. 1 patient has had spondylitis ankylopoietica.

Arthritis can start at any time after deflection of the fæcal stream via ileostomy if any part of the large bowel remains; the retention of the diseased rectal stump alone may precipitate the first attack. An initial attack was also seen after ileoproctostomy and was relieved only by rectal excision and institution of a permanent ileostomy. The condition responds readily within a few days of excision of the bowel provided this is not too long delayed.

There have been 3 deaths in this group. 1 of the 14 survivors did not respond to excision, having had arthritis for four years before operation. There was only a brief recurrence two months after operation in 1 of the remaining 13—7 of whom have reached five years—though 2 patients state that they feel an occasional "twinge" in the joints which were affected. The case of spondylitis is too recent for proper assessment.

Skin lesions.—The response to surgery was similar with skin lesions (9 cases), of which the commonest was erythema nodosum (7 cases). Only 1 patient had pyodema gangrenosum; herpes labialis was seen in 2. Stomatitis (6 patients) proved intractable until the bowel was removed; and it has not recurred since excision.

Eye complications.—These proved refractory, probably because they were of long standing before colonic excision, with considerable damage to eyesight from corneal ulceration (1 case) and iritis (1 case). The retina of 1 patient became detached; this received ophthalmic treatment with no further trouble after five years.

Venous thrombosis occurred preoperatively in 5 patients, in 1 of whom a cavernous-sinus thrombosis was successfully treated with antibiotics. The tendency to thrombosis has not recurred in the 4 patients who survive excision, 3 of them by five years.

Associated Conditions

Gastric ulcer and duodenal ulcer were observed, but they were no more prevalent than in the population in general (Doll and Avery Jones 1951). Psoriasis affected 3 patients, disseminated sclerosis 1, and polyneuritis 1.

Complications due to Surgery

Obstruction is a common complication immediately after ileostomy, and in most cases it passes off with expectant measures (Brooke 1954). As a late event, requiring readmission and laparotomy for relief, it has occurred in 7 patients—owing to a band in 6 (after ileoproctostomy in 1), and to intussusception in 1. In addition, 2 late deaths were due to obstruction.

Complications of the ileostomy.—These are the commonest late complications; they include prolapse, recession, stenosis, and fistula. Both prolapse and recession are due to detachment of the mesentery where it has been fixed in the para-ileal gutter (Brooke 1954), except when prolapse is part of an incisional hernia—a condition only encountered twice. Of the 106 patients in whom I fashioned the original ileostomy, 3 have had prolapse and 6 have had recession requiring operative correction. Skin-level fistula has developed in 3 at a late date from chaffing of the ileostomy bag. Stenosis occurred in about a quarter of the 35 patients in whom the ileostomy was formed by simple exteriorisation of the ileum, but since I introduced mucosal eversion with suture to skin (Brooke 1952), only 1 out of 71 ileostomies has become stenosed. This manœuvre has not predisposed to prolapse. In these 106 cases the opportunity was taken to revise the ileostomy at one of the staged procedures for excision in 9; and a further operation was required for revision alone in 4. 11 patients came to me with ileostomies already performed; in each the ileostomy was revised by me—at the time of an excision in 10. In some this revision was performed on account of a complication; in others because the original ileostomy had been undertaken before the advent of the adherent bag, and revision was necessary in order to enable the patient to use this appliance. The efficiency of the ileal stoma in this series therefore compares favourably with that reported by Bargen (1956) who states that only 14% of 124 patients were free of complications at the stoma within a year of operation, and that 43% of those surviving one year required revision. Ileal stomas are skin-grafted at the Mayo Clinic; this possibly raises the complication-rate.

Serious excoriation has occurred with recession and with skin-level fistulæ; but it has been cured after their correction. In 2 other cases rubber sensitivity, producing excoriation, developed after the rubber bag had been used for three years and for eighteen months.

Results and Conclusions

A complete review of all cases was undertaken in December, 1955. Patients have been placed in three groups, according to whether the first operation was five or more years ago, three to five years ago, or less than three years ago (table III).

TABLE III—FOLLOW-UP MATERIAL

Interval (years) since first operation	No. of patients	Deaths		Laparotomy only	Anastomosis unconverted	Ileostomy patients followed up at Dec., 1955		Ileostomy patients lost at Dec., 1955
		Op.	Late			Q.	I.	
5+	47	4	1	3	0	36	3	0
3–5	32	2	1	0	2	24	1	2
0–3	52	5	2	2	4	32	5	2
Total	131	11	4	5	6	92	9	4

Q = by questionnaire. I = interviewed.

The following questionnaire was sent to all surviving ileostomy patients except 9 seen personally at that time:

1. Are you well?
2. Are you at work at a job or household duties? How soon after operation did you return to work?
3. Can you follow your usual pastimes?
4. Do you find that your activities are limited in any way?
5. Is the ileostomy satisfactory?
6. What was your weight before operation and what is it now?
7. Do you limit your diet in any way and, if so, why?

Table IV shows that of 101 ileostomy patients followed, 92 are at full work, 7 being convalescent. The 2 patients

TABLE IV—FOLLOW-UP FINDINGS

—	Interval since first operation (years)			Total
	5+	3–5	0–3	
No. of patients ..	39	25	37	101
Health :				
Fit	37	23	30	90
Reasonable ..	2	1	7 (conv.)	10 (7 conv.)
Unfit	..	1	..	1
Work :				
Full	38	24	30	92
Limited ..	..	..	7 (conv.)	7 (7 conv.)
None	1	1	..	2
Pastimes : ..				
Full	35	19	25	79
Limited ..	4	6	12 (7 conv.)	22 (7 conv.)
Activities :				
Full	25	18	17	60
Limited ..	14	7	20 (7 conv.)	41 (7 conv.)
Ileostomy :				
Satisfactory ..	38 (4 exc.)	23 (3 exc.)	35 (4 exc.)	96
Unsatisfactory ..	1 (leak)	2 (exc.)	2 (exc.)	5
Weight :				
Gained	34	24	32	90
Stationary ..	2	..	3	5
Lost	3	1	2	6
Diet :				
Full	17	11	22	50
Restricted ..	19	14	11	44
Unstated ..	3	..	4	7

Conv. = convalescent ; exc. = excoriation of skin ; leak = leakage.

doing no work are nearly blind following iritis, 1 having arthritis in addition. 5 patients do not regard the ileostomy as satisfactory, though they do not go so far as to state that it is unsatisfactory, nor are they prevented from following full employment. 11 patients who consider the ileostomy to be satisfactory suffer slight or intermittment excoriation. Most patients are able to follow pastimes of their choice, such as swimming, dancing, and tennis ; old-time dancing is becoming popular ! The limitation in activity experienced by 34 patients is due to discomfort on stretching or bending, and sometimes when lifting heavy weights ; 7 others are still convalescent. Approximately half the patients restrict their diet, most because fruit-skins or pips form an indigestible bolus which causes colic as it reaches the indistensible ileostomy stoma. Some find that fruit-juices, green vegetables, or salads cause the motions to become fluid ; others avoid a large meal in the evening since this may so fill the adherent bag during the night as to require its evacuation. 6 patients are dieting in order to reduce weight which has increased embarrassingly (from 4 st. 7 lb. to 12 st. 8 lb. ; from 8 st. 8 lb. to 15 st.). The results remain satisfactory in those treated five years or more ago, 5 of whom have had an ileostomy for ten years or longer.

The fear has been expressed (Dennis 1945) that removal of the rectum might lead to impotence in the male. Specific inquiry on this point has shown the fear to be ungrounded—though it has not been possible to put the question to every male patient. 2 women have gone to term and breast-fed their babies after normal labour, without complication to the ileostomy ; another is approaching full term.

One disability has been encountered which arises out of a failure within the medical profession to appreciate the revolution wrought by the adherent ileostomy bag. Some patients when applying for jobs have been turned down on medical grounds. In contrast to this at least 1 patient has been accepted as a reasonable risk for life assurance.

The results indicate that patients submitted to permanent ileostomy are not incapacitated thereby, provided the ileostomy is efficient and designed for the use of the adherent bag. In this series only 2 of 101 survivors are not living a full life, and their permanent incapacity arises not from the ileal stoma but from a pre-existing complication of the disease. If surgery is undertaken soon after the onset of a complication this will be cured and will not recur.

One indication for surgery—which has been justified by the results—is this : that the time has come for operation when a patient appears unlikely to return to *normal* life after treatment by any other means.

Of 9 patients with anastomosis 3 have already required subsequent excision of the remaining bowel and permanent ileostomy, owing to either recrudescence or persistence of the disease in the rectum, and its complications. Those remaining are able to work and pass from two to eight motions in twenty-four hours, and 2 have intermittent anal excoriation. This method should not be regarded as a routine for surgical cure since remote complications do arise after resection ; and these may lead to incapacity which even full excision of the bowel, if delayed too long, will not correct. Resection and anastomosis has a limited application ; its indications have already been outlined.

Summary

131 patients with ulcerative colitis were operated on. 126 had elective operations (117 excision and permanent ileostomy ; 9 resection and anastomosis) with 15 operative and late deaths. This represents a mortality of 12% —about half the mortality of the disease treated conservatively in the pre-cortisone era.

The majority of late complications of operation arose in connection with the ileostomy. Eversion suture of the mucosa to skin is advocated to reduce the incidence of stenosis. Revision of the ileostomy was required in some cases to enable the patient to use an adherent ileostomy bag.

A follow-up, extending to five years and longer in over a third of the survivors, indicates that ileostomy should no longer be dreaded as an impediment to full, normal life ; indeed it restores patients with ulcerative colitis to full work, full weight, and an enjoyment of ordinary pastimes. In about half the patients the diet has to be restricted slightly. Ileostomy patients regard their ileostomies as satisfactory.

Resection and anastomoses with preservation of the anal sphincter (9 cases) has been less satisfactory in this series than excision and permanent ileostomy (117 cases). After sphincter-saving resection the disease may recur, and its complications may then arise for the first time. This method is not recommended as a routine, and its indications are limited : indeed, it is precluded for rectal hæmorrhage and perforation—complications encountered in this series.

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ACUTE RENAL FAILURE DURING PENTOLINIUM THERAPY

A. BARHAM CARTER
M.D. Camb., M.R.C.P.
PHYSICIAN

R. W. PAYNE
M.B. Camb.
JUNIOR REGISTRAR

ASHFORD HOSPITAL, MIDDLESEX

THE use of pentolinium in the treatment of severe hypertension has become widely accepted as an effective measure in controlling the height of the blood-pressure. Various side-effects are to be expected with such a powerful drug, but most of these are comparatively harmless and, in fact, useful in adjusting the dosage. Such effects are postural hypotension, dryness of the mouth, paresis of accommodation, and constipation, but more serious effects on the brain, heart, and kidneys may occur, even when caution is used. Two cases are described here of renal failure during treatment with pentolinium.

Case-reports

Case 1.—A man, aged 69, was first seen in September, 1954, with recurrent attacks of acute left ventricular failure associated with a blood-pressure of 230/150 mm. Hg. He also complained of headache and blurring of vision, and his fundi showed venous nipping, with tortuous arteries and retinal hæmorrhages. There was no exudate, although the edges of the discs were blurred. Electrocardiography showed a left ventricular strain pattern, and his blood-urea level was 60 mg. per 100 ml. The pressure was unchanged with rest, and, in view of the severity of the hypertension and the attacks of pulmonary œdema, it was decided to use pentolinium ('Ansolysen') and reserpine ('Serpasil'). He was eventually controlled satisfactorily on 200 mg. of pentolinium b.d. and 0·25 mg. of reserpine t.i.d., and his ambulatory pressure remained around 190–210 mm. Hg systolic and 100–110 mm. Hg diastolic. The urine was free from albumin, its specific gravity was 1·012–1·018, and its output good.

The patient remained well until Jan. 1, 1956 (fifteen months later), when he was seen by his general practitioner because of listlessness and drowsiness. The patient had noticed a reduction in the volume of urine the previous two days. His blood-pressure was 180/90 mm. Hg, and the doctor gave 2 ml. of mercurial diuretic intramuscularly. Next day the blood-pressure was 90/50 mm. Hg, and for twenty-four hours no urine had been passed. The patient was then admitted to hospital drowsy and mildly confused. Treatment consisted in feeding through a Ryle's tube with glucose solution according to the modified Bull régime, intramuscular methylamphetamine hydrochloride, and penicillin. Fig. 1 shows his progress and the electrolytic changes.

Case 2.—A man, aged 46, was admitted on Jan. 26, 1956, with four hours' history of sudden unconsciousness.

On examination he showed right hemiplegia, aphasia, and a blood-pressure of 240/160 mm. Hg. His fundi were grossly abnormal, with hæmorrhages and papilloedema, and his cerebrospinal fluid (C.S.F.) was clear and under a pressure of 280 mm. of water. His blood-urea level was 64 mg. per 100 ml., and his urine contained 90 mg. of protein per 100 ml., with no casts, the specific gravity being 1·014. There was some improvement in the neurological signs, but he remained confused, and his pulse-rate increased, and he began to show signs of acute pulmonary œdema.

Treatment.—In view of the severity of the hypertension and the signs of hypertensive heart-failure and encephalopathy it was decided to use pentolinium as an emergency. He had a strong dislike of injections; so on Feb. 1 he was given 50 mg. by mouth. There being no effect, a similar dose

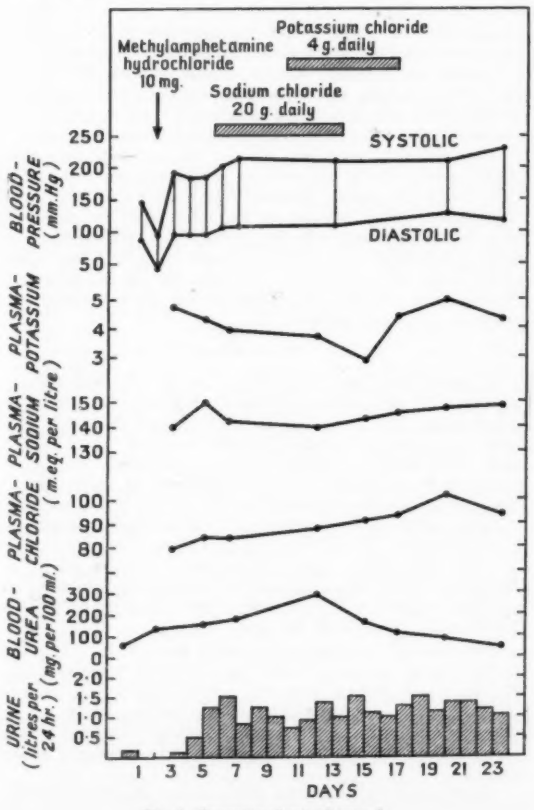

Fig. 1—Progress chart of case 1.

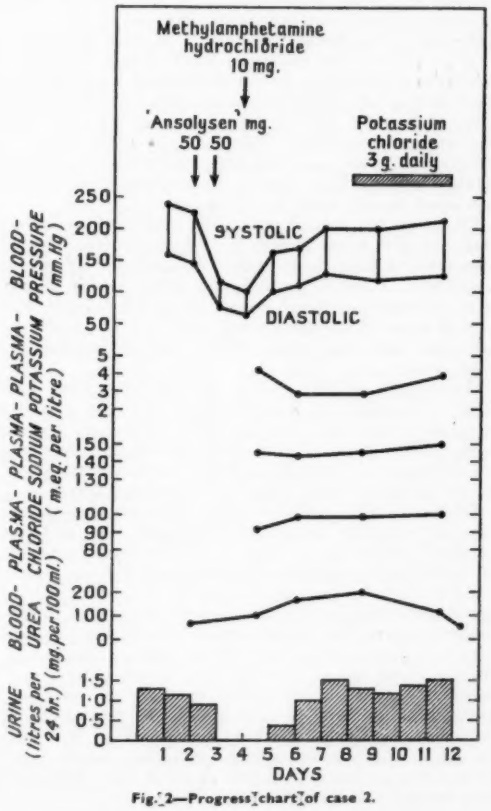

Fig. 2—Progress chart of case 2.

was given twelve hours later. The patient then gradually became unconscious, with periodic breathing, occasional hiccup, and only a slight response to painful stimuli. His pulse-rate was 60, blood-pressure 130/90 mm. Hg, and C.S.F. clear with a pressure of 240 mm. Five hours later there was no change and his blood-pressure was 90/70 mm. Hg and his pulse-rate 80. For twenty-four hours no urine had been passed, and his condition, at first thought to be due to encephalopathy, was recognised as hypotensive renal failure. Methylamphetamine hydrochloride 10 mg. was injected intramuscularly, and two hours later the systolic pressure was 120 mm. Hg and the patient was moving his arms, opening his eyes, and swallowing. His mental condition improved, but anuria continued for two days. He was treated by feeding through an intragastric tube with a glucose solution containing 400 g. of glucose in a litre of tap-water. He did not vomit, but his blood-urea level rose to 180 mg. per 100 ml. in forty-eight hours. He then began to pass urine again, and a week after the pentolinium therapy he had recovered completely. Fig. 2 shows the details of his illness.

Discussion

The type of renal failure developing in these two cases suggests an initial lowered filtration-rate associated with prolonged hypotension followed by failure of tubular function.

Case 1 shows the result of pentolinium therapy in an elderly man with reasonable renal function before treatment and apparently satisfactorily controlled for eighteen months. He then suddenly developed renal failure, shown by oliguria and drowsiness, and was not helped by an injection of organic mercury. Why his renal function should have failed in this way is not satisfactorily explained, but we suggested that his natural arteriosclerotic condition was progressive and therefore his renal function was slowly deteriorating all the time. In this way the pentolinium had an enhanced cumulative effect, bringing about a complete breakdown by lowering the renal filtration pressure.

In case 2 the cause is clearer. It was obviously an error to repeat the relatively high dosage (50 mg. by mouth) of pentolinium in twelve hours in a patient whose reaction to pentolinium was unknown, and it would have been much wiser to have given doses of 2·5 mg. or even 1·25 mg. parenterally. There can be little doubt that this patient could not deal adequately with pentolinium because he had no chance to acquire tolerance and developed severe renal hypotension.

There are few references to the effects of hypotensive drugs on the renal function of hypertensive patients; most reports have dealt with "controlled" hypotension in surgery. Hampton and Little (1953) report anuria in 54 of 549 cases in which complications developed in this type of case. This was part of a survey of 21,000 cases, and they note that renal failure was responsible for 8 of 46 deaths.

Mackinnon (1952), using pentamethonium iodide, obtained a reduction in renal blood-flow and glomerular filtration-rate with a rise in renal resistance, but Miles et al. (1952) reported that renal circulation was largely uninfluenced by the fall in blood-pressure brought about by the administration of pentamethonium bromide.

Wakim (1955) administered intravenously hexamethonium chloride to an anæsthetised dog and found prolonged reduction of renal blood-flow and of secretion of urine synchronous with the reduction of blood-pressure.

These two cases suggest firstly that the continued use of pentolinium tartrate may be dangerous to elderly patients, even although the usual side-effects of postural vertigo, constipation, dryness of mouth, &c., may be absent. The use of pentolinium in the elderly can be justified only as a life-saving measure in cases of left ventricular failure, progressive gross retinal changes, or continuing hypertensive encephalopathy. The patient should be instructed to watch for listlessness, drowsiness, or any diminution in volume of urine and thereupon to stop taking the tablets.

Secondly, if a patient requires urgent administration of a hypotensive drug, this should be given parenterally in the accepted small doses of 1·25–2·50 mg. and not in larger doses orally than has been recommended (Smirk 1953, Smirk et al. 1954). This mistake was made in case 2 owing to the patient's dislike of injections, and the consequences were very nearly disastrous.

The two cases show a fairly consistent clinical course. In case 1 the circulatory renal failure was of sufficient severity and duration to produce the changes of acute tubular necrosis which occur after experimental renal hypotension (Bull 1955). One of the most important effects of this is that, when urinary secretion is re-established, much potassium is lost, presumably through failure of tubular reabsorption of filtered potassium; but other mechanisms for this loss in renal disease have been suggested by Mahler and Stanbury, (1956). Case 1 was anuric for forty-eight hours, and his renal secretion was considerably reduced for a further forty-eight hours. His blood-urea and serum-potassium levels were already raised by then; and, although the blood-urea level rose still higher for twelve days, the serum-potassium level dropped steadily to 2·9 m.eq. on the fourteenth day but returned to normal fairly rapidly. The urinary potassium varied between 4 g. and 8 g. in twenty-four hours from the sixth to the seventeenth day of the illness.

A similar course was followed in case 2, but the anuria lasted only thirty-six hours. Here the serum-potassium level was never raised and dropped to 3·1 m.eq. per litre on the sixth day, and was restored to normal more quickly.

Treatment.—Once renal failure is suspected in a patient receiving pentolinium tartrate and the drug has been discontinued, it is important to restore circulation as quickly as possible by raising the blood-pressure. An intramuscular injection of methedrine sulphate 10 mg. was effective in each case, and care should be used in prescribing larger doses because hypertensive patients remain very susceptible to methedrine even when they are in hypotension. Once the blood-pressure has become reasonable, the treatment should be as for anuria from other causes, along the lines of Bull's régime (Bull et al. 1950), and the serum electrolytes need to be estimated frequently. The potassium loss can best be corrected with potassium chloride by mouth 1 g. six-hourly, but both potassium and sodium should be given cautiously (Bull et al. 1955). It is obviously unwise to return to pentolinium therapy in cases which have shown any evidence of renal failure.

Conclusions

In these two cases circulatory renal failure developed of sufficient severity to produce ischæmic changes in the renal cells. The histological appearances in this type of case are those of acute tubular necrosis (Bull 1955); and, once renal secretion begins again when the blood-pressure is restored, the consequences of this necrosis become apparent. Presumably the longer the circulatory failure continues the more severe will be the renal necrosis and its effects. In addition, owing to previously prolonged hypertension, the renal vulnerability to changes in the circulation will be increased, and so the margin between effective control of hypertension and lowering of efficient renal circulation must be quite small.

Two points particularly emerge from this. The first is that renal function should be estimated before starting radical hypotensive therapy. Probably a combination of the thirst concentration test; examination of the urine for albumin, casts, and red cells; and estimation of the blood-urea level will give the most helpful assessment.

The second point is that the patient should be warned of the importance of any diminution of urinary secretion

while he is taking powerful hypotensive drugs. He will need to be taught the difference between suppression and retention, both of which may develop.

Summary

Two cases of acute renal failure during the treatment of hypertension with pentolinium tartrate ('Ansolysen') are described.

This complication may arise without other side-effects of pentolinium.

In hypertensive patients showing evidence of decreased renal function, powerful hypotensive drugs should be used only as a life-saving measure.

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TRANSFER OF RADIOSODIUM TO HUMAN FŒTUS IN LATE PREGNANCY

C. G. CLAYTON
M.Sc.
PHYSICIST, ROYAL VICTORIA INFIRMARY, NEWCASTLE UPON TYNE

F. T. FARMER
Ph.D. Camb., F. Inst. P.
PRINCIPAL PHYSICIST, NEWCASTLE REGIONAL HOSPITAL BOARD

TREVOR JOHNSON
M.D. Lond., F.F.A.R.C.S., M.R.C.O.G.
FIRST ASSISTANT, DEPARTMENT OF OBSTETRICS AND GYNÆCOLOGY, KING'S COLLEGE, UNIVERSITY OF DURHAM

From the Department of Obstetrics and Gynæcology, King's College, University of Durham, and the Radiotherapy Department, Royal Victoria Infirmary, Newcastle upon Tyne

IN normal pregnancy placental efficiency reaches its peak by the 36th week of gestation and diminishes progressively thereafter (Cox and Chalmers 1953b). This fact has been held responsible for the increased fœtal mortality when pregnancy is prolonged for more than 14 days after the expected date of confinement. The death of the fœtus is attributed to intra-uterine anoxia (Walker and Turnbull 1953).

This onset of placental failure is often accelerated in pregnancies complicated by either pre-eclampsia or essential hypertension, and the resultant changes within the placental villi and maternal decidua are ischæmic. The altered placental blood-flow has been measured by Browne and Veall (1953) and the uterine blood-flow by Morris et al. (1955), using tracer doses of radioactive sodium.

The best time for intervention to save these anoxic infants is difficult to decide from ordinary clinical signs, and it is clear that a practical method of assessing placental function before the onset of labour will introduce a new precision into the management of such cases.

The general nature of the mechanism of transfer of radiosodium (^{24}Na) from mother to fœtus during parturition and the significance of the results obtained by Flexner and Pohl (1941), Flexner et al. (1948), Browne and Veall (1953), Cox and Chalmers (1953a), and Johnson and Clayton (1955) in both normal and abnormal pregnancies and labours led us to consider the possibility of measuring antepartum placental transfer-rates with apparatus mounted externally to the pregnant uterus. The apparatus is arranged to detect the accumulation, within the fœtus, of tracer amounts

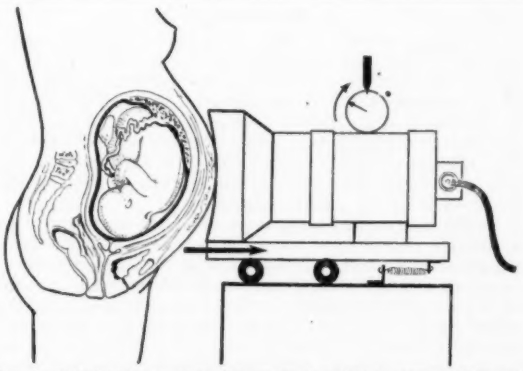

Fig. 1—Scintillation-counter for measuring fœtal accumulation of radiosodium.

of ^{24}Na administered to the mother, and placental function is assessed from comparative rates of uptake of labelled sodium in normal and abnormal pregnancies.

Experiments were made with a screened collimated scintillation-counter mounted vertically over the uterus with the patient supine and, to make intermittent observations over several hours, with the counter horizontal and the patient standing in front of it with her uterus firmly pressed against it (fig. 1).

We have attempted to assess the value of this technique for measuring placental function antepartum. The simpler appearance of the pattern of sodium transfer which results from a technique using external measurements and the ability to make multiple observations on the same fœtus overcomes the previous difficulty of obtaining only a single measurement for each infant (Flexner et al. 1948, Johnson and Clayton 1955) and is at the same time independent of most variations in fœtal and maternal extracellular spaces.

Owing to the relative sizes of mother and fœtus one of the chief difficulties of this approach to the measurement of fœtal transfer-rates is that of detecting the small differences between the initial radiosodium level at a point over the maternal abdomen when only the sodium space of the mother contains the isotope, and the radiation level at the same point when equilibrium has been reached between maternal and fœtal radiosodium concentrations. We have considered several arrangements and find a single lead-collimated scintillation-crystal counter most suitable.

In addition, consideration was given to variations in the position of the fœtus relative to the counter. Not only is it possible for the distance to vary considerably between the fœtus and the mother's anterior abdominal wall, but also almost any orientation of the fœtus within its sac is possible. These variations preclude the design of a collimating system which will differentiate precisely between fœtal and maternal radioactivity. If, for example, the fœtus is small and the mother obese, most of the recorded radiation will originate in the surrounding maternal tissues; whereas, if the fœtus is large and immediately beneath a thin maternal abdominal wall, its radioactivity will contribute a greater proportion of the total radiation measured by the counter.

We are attempting to solve this problem at present by studying the time taken for the increasing fœtal radioactivity to reach half its final equilibrium value, the full level being reached in about 3 hours after injection of the isotope.

We believe that with a technique of this type quantitative figures for radiosodium transfer can be obtained (see below). Not all the problems, however, have yet been overcome.

Rationale

If a small volume of isotonic saline containing radiosodium is injected intravenously, the radiosodium is equally distributed throughout the maternal plasma in about a minute and diffuses thereafter into the extracellular spaces of the different tissues (Gellhorn et al. 1944, Flexner et al. 1948, Cox and Chalmers 1953a, Johnson and Clayton 1955). In pregnancy it also crosses the placenta and is carried into the vascular system of the fœtus by the fœtal cardiac action.

So far as external measurement of the radiation with a counter placed over the trunk is concerned, the non-pregnant body can be considered as a constant source; hence at a short distance away from the body the amount of radiation is independent of the various processes taking place within the body. Local diffusion into the extracellular spaces, for instance, makes no difference to the total count, provided that the diffusion is taking place uniformly throughout the body (see fig. 2, which records

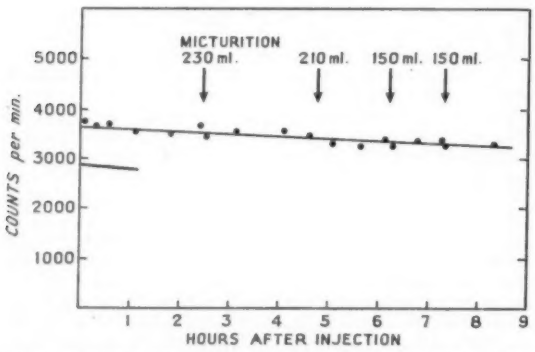

Fig. 2—Abdominal radioactivity of two non-pregnant women after intravenous injection of radiosodium.

radioactivity over the abdomen of two non-pregnant women for 52 minutes and for 8 hours after injection).

The fact that the measured radioactivity corrected for decay remains substantially constant in such cases strongly suggests that any increase in radioactivity recorded over the abdomen of a pregnant patient is due to the passage of radiosodium into the fœtus, which initially has no radiosodium and gradually acquires radiosodium at a rate which depends on the condition of the placenta and its environment. The increase in radioactivity will then be a measure of the radiosodium transferred to the fœtus. In a pregnant woman the "background" radiation will decrease very slightly during this transfer, owing to loss of radiosodium from the mother to the fœtus, with concurrent "slow-phase" diffusion into the extracellular space of the maternal central nervous system and bone (Fauvert and Loverdo 1950) and excretion by the kidneys and sweat-glands. This diminishing local radioactivity is observed in the non-pregnant woman (fig. 2) and might be allowed for by applying a second counter over these parts, but we have not yet attempted systematic correction along these lines.

The time required for the radiosodium levels of mother and fœtus to reach equilibrium has been shown by ourselves and others to be at least 3 hours. If, therefore a counter is placed over the pregnant abdomen as in fig. 3 and the radioactivity is measured at intervals of a minute, its increase will indicate the efficiency of the placental transfer of radiosodium. If this increase is rapid, with an appreciable increase in counting-rates in the first 40 minutes, it means that the transfer is good; but if the increase is slow, with little change in the first 40 minutes, the transfer is poor.

From these observations alone it is impossible to state a value for the transfer efficiency, because the rate of increase depends on the size of the fœtus, its distance from the maternal skin, and the fraction of it embraced by the angle of the counter (fig. 3). However, if we use the time taken by the fœtus to acquire half its final radiosodium level as the figure of merit for placental efficiency, this gives a unique value independent of all the above-mentioned geometrical factors. Fig. 3 shows that, when the counter and the fœtus are close together, there is a large difference between the radiation level measured at the time of injection and that measured when the radiosodium levels of mother and fœtus have reached equilibrium. When, however, the counter and the fœtus are well separated, there is a much smaller change between the initial and the final radiosodium levels, even if the transfer efficiency proves to be the same. By placing the counter as close to the skin as possible, permitting a small degree of compression, and by collimating it towards the centre of the fœtus, the increase in the counting-rate can be made maximal.

The only time this technique gives a faulty result is when the fœtus moves its position during the observation period or the counter does not remain in an exactly constant relationship to the mother's abdomen. As already mentioned, in our earlier experiments the patient lay supine with the counter held vertically above the anterior aspect of the uterus and in close contact with the abdominal skin. It was usually found impracticable to make observations for longer than an hour in this position, owing to the discomfort experienced by the patient and to her anxiety from the proximity of heavy apparatus. The counting-time was insufficient for maternal fœtal equilibrium to be reached, and as a result we have recently changed the technique so that the axis of the crystal and the collimator is horizontal, with the mother standing in front of it. To maintain constant separation of the scintillation-crystal and fœtus, the entire radiation-detecting apparatus, including crystal, lead collimator, and photomultiplier housing, have been mounted on small wheels and spring-loaded (fig. 1). Once the height of the standing patient has been adjusted to centre the fœtus over the crystal, the patient is requested to push against the apparatus to produce a comfortable degree

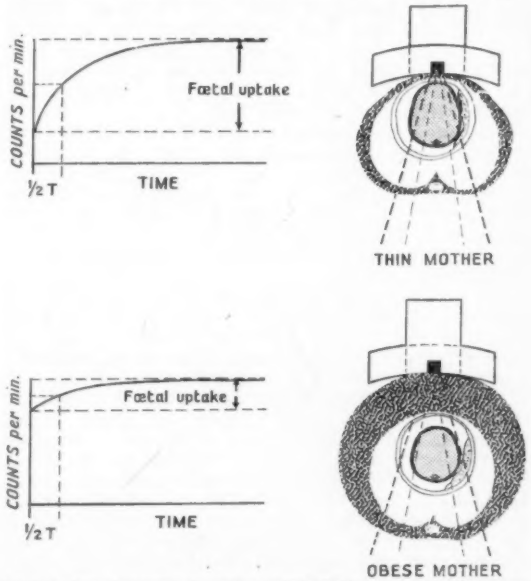

Fig. 3—Effect of obesity of mother and size of baby on radiation-count with equal placental efficiency.

of compression. This is observed by the patient on a simple spring-operated indicator, and is easily repeated at subsequent readings. By this means $^1/_2$-minute counts are made every few minutes for an indefinite period, without significant discomfort to the patient, who rests in a chair between each measurement.

Method

5·0 ml. of isotonic saline solution containing about 20 μC. of ^{24}Na was injected into the right antecubital vein. (The total exposure of mother and fœtus to radiation after this dosage is about 0·01 rad., which is considerably less than the prescribed safety limit [*British Journal of Radiology* 1951].)

The abdominal radioactivity was measured by a scintillation-counter consisting of a thallium-activated cylindrical sodium-iodide crystal 1·2 cm. in diameter and 2·5 cm. long set in a large lead collimator. The crystal was in contact with the photocathode of an electron multiplier which in turn was connected to a standard scaling apparatus and register. The change in radioactivity was observed from measurements made for $^1/_2$ minute at intervals of 2–20 minutes over 3 hours. The highest counting-rate over a typical abdomen was

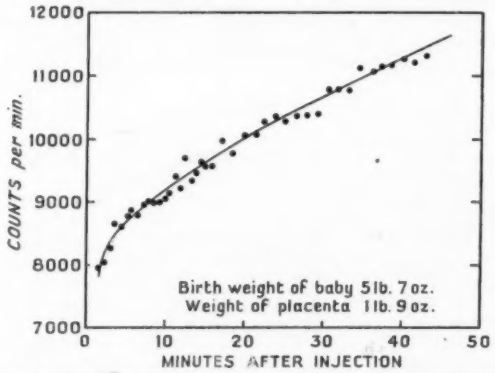

Fig. 4—Fœtal accumulation of radiosodium in uncomplicated pregnancy of thin mother subsequently delivered of small baby.

about 8000 counts a minute, and the background count of the room was 50 counts a minute.

2 minutes after the intravenous injection the site of the injection was tested for radioactivity with a Geiger-Müller tube and counting-rate meter, and compared with the radioactivity of the corresponding site in the left arm. In no case was any residual radioactivity recorded.

To test the apparatus and to show that, when the radioactivity was constant, the recorded counting-rate remained constant, radioactivity of a radiosodium standard was measured from time to time. Although we found that micturition had very little effect on the total abdominal count (fig. 2), the patient emptied her bladder before starting the experiment, to avoid any variation in background during the observations.

Results

These are based upon 61 consecutive experiments, the patients being classified into the four separate groups as follows :

Clinical material	*No. of cases studied*	
	Vertical counter	*Horizontal counter*
Non-pregnant	7	1
Uncomplicated full-term pregnancies	15	6
Intra-uterine deaths	4	2
Pre-eclampsia (including repeated examination at weekly intervals)	1	25

Representative graphs for each category show the fœtal accumulation of radiosodium after the intravenous injection of 20 μC. radiosodium in isotonic saline solution into the mother. Appropriate corrections have been made for the decay of radiosodium during each experiment. Relevant clinical data at the time of the investigation and at subsequent delivery are included with each curve. An additional graph (fig. 6) shows how fœtal movement affects the count.

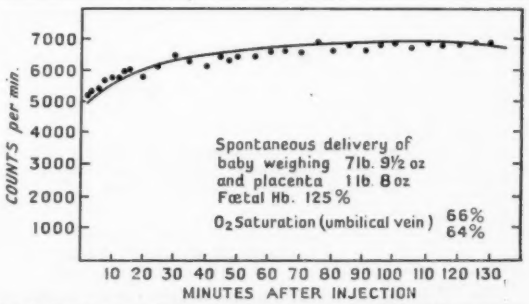

Fig. 5—Fœtal accumulation of radiosodium in uncomplicated pregnancy of obese mother subsequently delivered of fair-sized baby.

Non-pregnant

Fig. 2 has already been referred to above and is typical of the results we have obtained in every investigation on non-pregnant women. It shows that the abdominal radioactivity slowly decays owing to diffusion into distant structures—e.g., central nervous system and the skeleton. The simultaneous loss of radiosodium in sweat and urine has been shown by Cox and Chalmers (1953a) to be about 0·14% hourly of the total quantity administered ; this is consequently not an important source of error.

Uncomplicated Full-term Pregnancy

Fig. 4 shows the results obtained in a full-term pregnancy 24 hours before normal delivery. The patient was slender, and the infant, which subsequently weighed 5 lb. 7 oz. at birth, was readily palpable (cf. fig. 3).

Fig. 5 shows the results obtained in a relatively obese mother and a fair-sized infant which subsequently weighed at birth 7 lb. $9^1/_2$ oz. The thickness of the maternal abdominal wall and the distance of the baby from the counter are reflected in a small increase of radioactivity which correlates with the geometrical data (cf. fig. 3). The patient was delivered spontaneously 24 hours after the experiment, and the oxygen saturation and hæmoglobin levels in the umbilical venous blood at this time were compatible with normal placental action (Walker and Turnbull 1953).

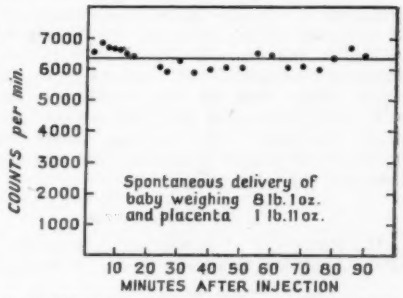

Fig. 6—Effect of fœtal movements on radiation-count.

Fig. 6 shows the effect of movements of the fœtus on the radiation-count in an uncomplicated full-term pregnancy (delivery took place spontaneously 24 hours later, the infant weighing 8 lb. 1 oz.).

Intra-uterine Death

Fig. 7 is a typical example of a curve obtained from an unexplained intra-uterine death at the 33rd week of pregnancy, the patient being delivered 8 days later of a macerated infant weighing 2 lb. 8 oz. and a placenta weighing 14 oz. Owing to the complete absence of

fœtal uptake of radiosodium the curve has the characteristics of one obtained from a non-pregnant woman (cf. fig. 2).

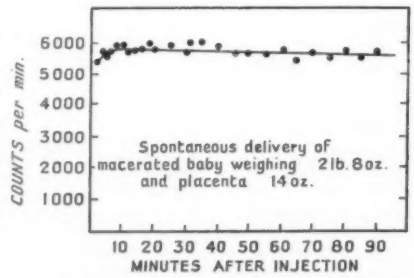

Fig. 7—Complete absence of uptake of radiosodium by fœtus indicates intra-uterine death.

Pre-eclampsia

An unmarried primigravida, aged 16, was an emergency admission at the 31st week of pregnancy with severe pre-eclampsia, blood-pressure 140/95 mm. Hg, generalised œdema of face and limbs, and albuminuria 1 g. per litre (Esbach). Although the œdema and hypertension lessened with treatment, the albuminuria steadily increased to 2 g. per litre at the 33rd week and 3 g. per litre at the 34th week of pregnancy, and the uterus remained considerably smaller than is usual for this duration of pregnancy. Fig. 8 shows the diminishing rates of uptake of radiosodium by the fœtus at the 32nd, 33rd, and 34th weeks of pregnancy. Intra-uterine death took place 3 days after the last observation, and the patient was delivered of a stillborn infant weighing 2 lb. 13 oz. at the 35th week of pregnancy. There was no residual evidence of either hypertension or albuminuria when she was discharged from hospital on the 18th day of the puerperium.

A secundigravida was admitted to hospital at the 39th week of pregnancy with fairly severe symptoms of pre-eclampsia. There was no clinical œdema, but her blood-pressure was 150/100 mm. Hg, and she had albuminuria $1^1/_2$ g. per litre (Esbach). The fœtal uptake of radiosodium at this time (fig. 9) compared with the uptake a week later shows evidence of deteriorating placental efficiency, which is correlated with an increase in the maternal albuminuria to 3 g. per litre. Labour was induced surgically at this time, and the patient was delivered of a living male infant weighing 7 lb. 10 oz. after labour lasting 11 hours. The raised level of hæmoglobin in the infant's venous cord-blood (150%), the oxygen saturation of 48%, and meconium staining of the liquor amnii were all confirmatory evidence of fœtal anoxia and disturbed placental action, which had been previously suspected from an antepartum reduction in the fœtal uptake of radiosodium and from worsening maternal pre-eclampsia.

Conclusions

If a tracer dose of radiosodium is injected intravenously into a pregnant woman in the latter weeks of pregnancy, its rate of accumulation within the fœtus can be observed with a collimated scintillation-counter placed over the centre of the anterior aspect of the pregnant uterus.

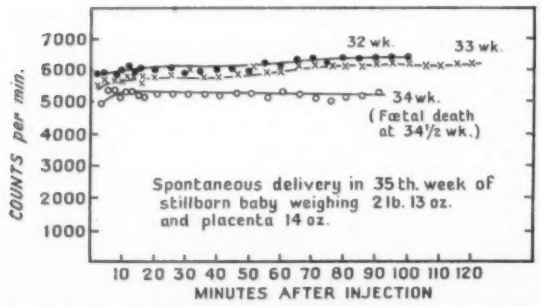

Fig. 8—Diminishing uptake of radiosodium by fœtus in pre-eclampsia.

The time taken for the radiosodium level of the fœtus to reach half the level of equilibrium with the maternal plasma can theoretically be used as a direct quantitative index of placental efficiency, and this value is independent of the geometrical relationships between mother and fœtus. In practice, however, we cannot yet give a reliable value for this single placental figure of merit.

The measurement of placental efficiency by a counter placed externally to the mother allows an almost unlimited number of observations to be made on the fœtus instead of a single measurement at the time of delivery, as in methods previously described.

The technique can be used repeatedly antepartum in any individual case and with complete safety and relatively minor discomfort to the mother.

Intra-uterine deaths from insidious injury to the placenta in the latter weeks of pregnancy will be lessened by more accurate assessment of placental efficiency.

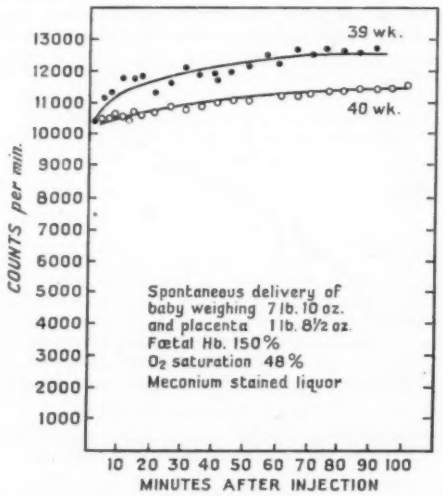

Fig. 9—As fig. 8.

Even in this early stage of development our technique yields valuable information, especially if more data than this single parameter are used to assess the results. Furthermore, the above-mentioned geometrical variations assume less importance in successive weekly observations on the same patient to identify quantitative changes in placental efficiency.

Although this technique yields evidence of the more insidious type of placental ischæmia sometimes found in hypertensive mothers, it seems unlikely that the abrupt deterioration of placental action which accompanies accidental hæmorrhage will be as readily predicted, unless there is preceding pre-eclampsia.

The method has proved completely reliable as a means of diagnosing fœtal death in the cases studied so far, a positive result being obtained as soon as the infant dies and long before confirmatory radiological evidence is possible.

Future technical developments in the useful application of radioactive substances to this problem of placental physiology will depend on close collaboration between obstetrician and physicist.

We are indebted to the continued encouragement of Prof. Harvey Evers and Mr. C. J. L. Thurgar and the generous help of a research grant from the Newcastle upon Tyne Regional Hospital Board.

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TEA-DRINKING AND GASTRITIS

FELICITY C. EDWARDS
B.M. Oxfd, M.R.C.P.
CLINICAL RESEARCH ASSISTANT, WEST MIDDLESEX HOSPITAL, ISLEWORTH

JOHN H. EDWARDS *
M.B. Camb., M.R.C.P.
LATE SENIOR HOUSE OFFICER, CENTRAL MIDDLESEX HOSPITAL, LONDON

IT is reasonable to suppose that exposure to temperatures capable of damaging the surface of the body would be harmful to its interior, and that the ingestion of hot foods and fluids may be a contributory cause of disease of the upper digestive tract. Such disease is far commoner in man than in animals, and the heating of foodstuffs is one of the most widespread attributes exclusive to man. Further, there is no reason to suppose that heat, if painless, is also harmless; for the very short history of cooking is obviously insufficient to have occasioned the evolution of an appropriate sensory apparatus.

Few observations have been made on the temperature of food either in health or in disease. The observations presented here were made in order to explore the hypothesis that the intake of drink at high temperatures is positively associated with mucosal abnormalities in the stomach.

Material and Methods

A good opportunity arose when a series of 155 patients (109 men and 46 women) with indigestion, all of whom had had successful gastric biopsy at some time during the previous three years, were being interviewed. Biopsy specimens had been taken by means of a modified flexible Australian instrument (Wood et al. 1949, Coghill and Williams 1955), two or more specimens usually being obtained, in most cases from different levels of the body of the stomach. The mucosa was subsequently classified into four groups: normal, miscellaneous (changes consisting mainly of an apparent excess of inflammatory cells in the stroma), chronic superficial gastritis, and chronic atrophic gastritis (Coghill and Williams 1955). In the 14 cases where more than one histological diagnosis was made, the case was classed under the most severe.

Towards the end of the interview the patient was given a fresh cup of boiling tea, made separately each time, with milk and sugar added if usually taken, and was asked to sip it frequently. When it had cooled to the temperature at which it was usually drunk (i.e., taken quickly in successive gulps), this was recorded. With very few exceptions the observer recorded the temperature in ignorance of the histological report. The observation was made only once for each patient. The thermometer used was graduated in intervals of 2°F. It was assumed that the individual elects to swallow different hot foods and drinks at much the same temperature; but this assumption is not necessary to substantiate the significance of the present findings.

Results

The accompanying figure gives the data, together with estimates of the mean temperatures, the standard deviation, and the standard error of the mean, for each histological grade. Age had no evident effect, apart from an apparent negative association in normals, explicable by a more rapid increase in the prevalence of mucosal abnormalities with age in those who drink hotter tea. There was no definite sex difference, men taking tea 0·9 ± 1·5°F hotter than women.

A progressive rise in the mean temperature over the different histological grades is apparent, the upward trend being associated with increasing abnormality of the mucous membrane. The prior decision, made in the false expectation of a positive association of temperature and age, to assess the significance by commuting the independent probabilities for age-groups 15–30, 31–45, and 46+, each being assessed by students "t" test for one tail, all abnormalities being classed together, showed significance at the 1% level (see accompanying table).

Although no other significance test is rigorous, the trend, and the great difference in mean temperature between the extremes of mucosal type—a difference 3·89 times its standard error (an event which would be expected, through chance, less than once in ten thousand sets of data)—strongly support the assumption that contemporary drinking habits may be associated with histological change. While it is always easy to make exaggerated claims by selection of data, it is nevertheless of interest that, considering persons under the age of 50, only 2 of the 13 drinking tea below 122·5°F showed mucosal abnormalities; while of those drinking it above 137·5°F, 14 out of 18 had an abnormal mucosa.

The taking of biopsy specimens, the cutting and reporting of the sections, the drinking of tea, and the measurement of temperatures, are all liable to variation and observer error. From the design of the survey there can have been no bias, except in the few cases where the observer could be held to have some memory of the biopsy reports. However there was no significant digit preference at five divisions for each ten degrees, and the prior expectations of age and femaleness being positively associated with drinking hotter tea were not realised. The fact that the specimen-taking, histological grading, thermometry, and the patients' assessment of their habitual oral temperature preference for tea may not be strictly reproducible, in no way impairs the logical implications of the data; on the other hand, the greater the degree of observer errors involved, the more distinct must be the association of heat and damage to lead to significant discrepancies.

RELATION OF HISTOLOGICAL APPEARANCES (NORMAL OR ABNORMAL) TO AGE

—	Age (yr.)					
	15–30		31–45		46–80	
	Normal	Abnormal	Normal	Abnormal	Normal	Abnormal
No. of patients	13	5	31	15	34	57
Mean temp. (°F)	133·077	135·200	127·548	134·000	127·235	132·988
S.D.	5·267	7·430	7·445	7·746	8·778	9·063
Δ	2·123		6·452		5·753	
t	+ 0·6870		+ 2·717		+ 2·899	
p	0·25		0·005		0·004	
Commuted p	<·01					

* Present address: Department of Social Medicine, University of Birmingham.

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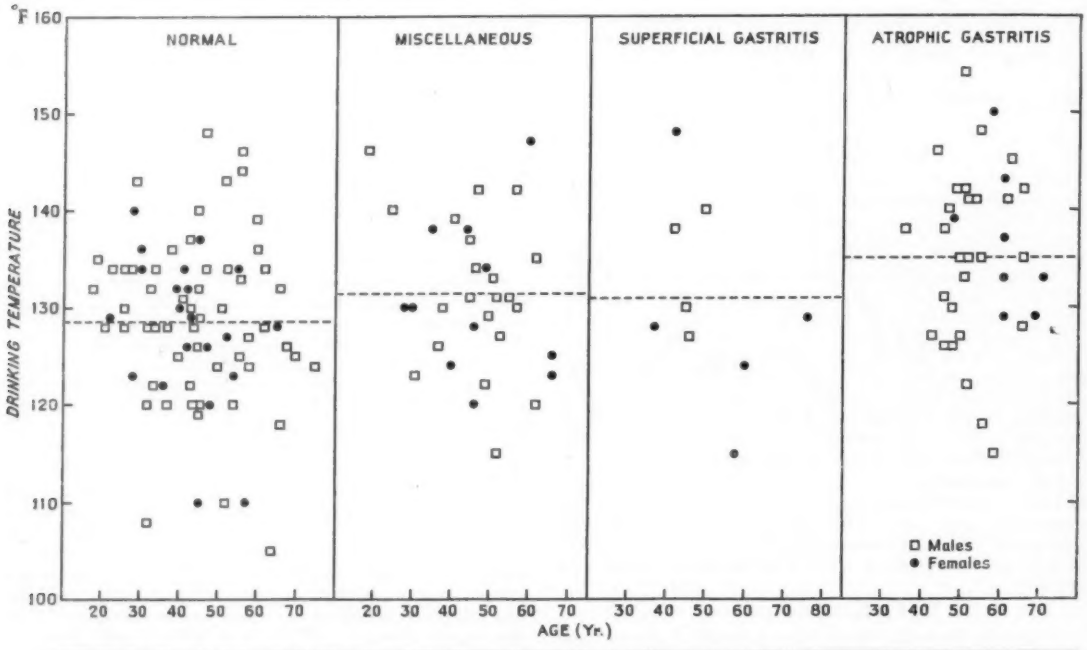

	NORMAL	MISCELLANEOUS	SUPERFICIAL GASTRITIS	ATROPHIC GASTRITIS
NUMBER	78	32	9	36
MEAN	128·49°	131·25°	130·78°	135·11°
S.D.	7·49°	7·70°	9·81°	8·85°
S.E. of MEAN	0·85°	1·36°	3·27°	1·48°

Age and sex of patients, drinking temperature, and biopsy findings.

Discussion

Hunt (1947), using a similar method with 236 healthy students, found a higher mean temperature of choice (140–142°F), and also a somewhat higher standard deviation (11°F). This is possibly due to his use of a beverage infrequently drunk ('Oxo'). Hepburn et al. (1933), Eberhard (1940), and Davis and Ivy (1949), who measured oral temperature tolerance (i.e., the maximum temperature at which foods or fluids can be taken without undue discomfort) for hot drinks, recorded ranges of 124–154°F, and 113–149°F in smaller numbers of students.

Several workers have postulated an association between hot food and gastric disease, particularly carcinoma and peptic ulcer. Van Valzah and Nisbet (1896) considered that cooks had a high incidence of peptic ulcer, and Heiser (1922) reported that the majority of his ulcer patients ate quickly or ate hotter food than normal. Argentinians are popularly supposed to take their food at temperatures approaching 80°C (176°F) and are known to have a high incidence of œsophageal carcinoma (Davis and Ivy 1949). In 1936 Herbert and Bruske, in their survey of environmental differences relevant to the higher recorded incidence of gastric cancer in Holland than in England and Wales, estimated that 22% of Englishmen, compared with 43% of Dutchmen, habitually took food and drink at temperatures over 60°C (140°F), suggesting a mean temperature of choice of about 133°F and 138°F in the two countries respectively. Mann et al. (1939), in a similar survey enlarged to include Sweden, concluded that only 14% of the 500 Swedes concerned took food and drink over 60°C, suggesting a mean temperature of choice for Sweden of about 132°F. An entirely qualitative survey by Dunham and Brunschwig (1946), reviewing the dietary and related habits of patients with and without gastric carcinoma, indicated that 42·5% (17) of cases with gastric neoplasms admitted taking their food hotter than the rest of their families, as compared with only 20% (8) of controls, most of whom had other abdominal disorders.

An alternative approach to the study of this relationship is provided by work dealing with attempts to produce gastric lesions with hot fluids and foods. In 1887 J. Decker (cited by Davis and Ivy 1949) tube-fed dogs gruel at 62°C (144°F) and produced acute mucosal erosions and hæmorrhages. J. H. Lewis (cited by Wells et al. 1938) fed hot mush daily through the gastrostomies of 35 dogs; none of the animals survived for more than a year, and none showed evidence of gastritis, peptic ulcer, or gastric carcinoma post mortem. Ivy and Farrell (1926) produced temporary achylia gastrica in dogs by placing water at 70–75°C (158–167°F) into their gastrostomies, and were able to maintain the achylia by repeating the process weekly; but no histological data are included in their paper. Dyer et al. (1946) failed to produce chronic gastric lesions in mice by administering hot water orally; the only lesions seen after death were acute hæmorrhages into the gastric mucosa. The average survival-time of the mice was between six and seven months, and it is unfortunate that the value of these experiments and of those of Lewis is lessened by their relatively short duration. In further experiments Davis and Ivy (1949), studying acute thermal damage in the stomachs of anæsthetised dogs, produced minimal detectable injury with water applied at 122°F for ten minutes, and at 131°F for five minutes. Repeated daily doses of hot water were reported in two of the dogs to produce microscopic changes suggestive of chronic gastritis, but unfortunately details of these latter experiments are not given. Recently Y. Hirai (cited by Ivy

1955) is said to have succeeded in producing gastritis, with evidence of hyperplasia and hypoacidity, by feeding dogs food at 46·3°C (115°F) over long periods.

Our data, and many of those referred to above, suggest that heat may be a common cause of pathological change in the gastric mucosa. It seems probable that diseases of the stomach are related to many factors, some local, some innate, and some due to general environmental effects. It is unlikely that any one factor in gastric disease will be found to be either a sufficient or a necessary cause in the majority of cases; but however many factors there may be, the elucidation of one which can easily be avoided may sometimes make possible a reduction in the total noxious stimuli to below the threshold of symptomatic, or even precancerous, disease.

Summary

In 155 cases of indigestion in which gastric biopsy had lately been done, tea-temperature preferences were investigated.

There was clear evidence of association between the chosen drinking temperature and mucosal abnormalities which is not explicable on grounds of sex or age.

This association is probably causal, and thermal injuries to the gastric mucosa may be very common.

We wish to thank Dr. N. F. Coghill, of the West Middlesex Hospital, whose patients coöperated in this survey, and Dr. A. Wynn Williams, of the pathology department, University of Edinburgh, who reported on the sections.

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THE RELATION BETWEEN SMALLPOX VACCINATION AND POLIOMYELITIS

H. D. CHALKE
O.B.E., M.R.C.P., D.P.H.
MEDICAL OFFICER OF HEALTH FOR CAMBERWELL; DIVISIONAL MEDICAL OFFICER, LONDON COUNTY COUNCIL

F. L. CLARK
B.A.
DIVISIONAL ADMINISTRATIVE OFFICER, LONDON COUNTY COUNCIL

MacIver (1956) produced evidence which suggested that in young children vaccination * may confer some protection against paralytic poliomyelitis. On the other hand, an inquiry in Vienna (Berger and Puntigam 1956) into the vaccination state of 111 children under 4 years of age, who contracted poliomyelitis in the years 1951–55, yielded no substantial support for this hypothesis.

We have analysed the records of 57 notified cases of paralytic poliomyelitis in children under 5 years of age, in a health division of the County of London, which has 29,300 children under 5 years old.

Table I shows that 54% of these children had been vaccinated—a proportion higher than the vaccination-acceptance rate for the area (47%). The preponderance of vaccinated children is in the 2–4 age-group and in the 1955 children, and is largely due to 5 vaccinated children between 2 and 4 years of age who contracted the disease in August, 1955.

* In this paper, "vaccination/vaccinated" means vaccination/vaccinated against smallpox.

TABLE I—VACCINATION STATE OF CHILDREN AGED 0–5 YEARS WHO CONTRACTED PARALYTIC POLIOMYELITIS IN 1951–55

Age at onset (years)	Vaccinated	Unvaccinated	Year of onset	Vaccinated	Unvaccinated
0–1	3	5	1951	1	..
1–2	8	11	1952	3	5
2–3	7	4	1953	8	9
3–4	8	1	1954	3	2
4–5	3	4	1955	14	9
0–5	29*(54%)	25 (46%)	All years	29*(54%)	25 (46%)

* In 3 of the 57 cases, vaccination details were not traced leaving 54 in the survey.

Table II shows that there was usually a longish interval between vaccination and the onset of poliomyelitis.

Table III shows the vaccination history of the 29 poliomyelitis children for whom we were able to find, in the central birth-notification index, control children of the same sex who were closely matched for age. (The differences permitted were one month where the poliomyelitis child was under 6 months old, two months where the child was 6–17 months old, and three months where the child was 18 months old or more.) In total, there is no significant difference between cases and controls.

TABLE II—RELATION BETWEEN AGE OF VACCINATION AND AGE OF ONSET

Age of onset (years)	Age of vaccination (months)	Period between vaccination and onset (months)
0–1	3, 3, 3	1, 5, 8
1–2*	3, 3, 3, 4, 9, 9, 17	4, 5, 7, 9, 12, 18, 19
2–3	3, 3, 7, 8, 8, 8, 16	8, 17, 18, 21, 22, 27, 32
3–4*	3, 3, 4, 5, 6, 6, 22	19, 32, 33, 34, 35, 37, 40
4–5*	8, 36	12, 47

*Excluding one case in which month of vaccination was not recorded.

Though these figures, taken as a whole, afford no evidence that vaccination has a protective action against paralytic poliomyelitis, the numbers are too small to allow of any firm conclusion. Surveys on a much larger scale should be undertaken, and it would be particularly

TABLE III—HISTORY OF VACCINATION IN CASES OF PARALYTIC POLIOMYELITIS AND IN MATCHED CONTROLS

—	Poliomyelitis cases		Controls	
	Vaccinated	Unvaccinated	Vaccinated	Unvaccinated
Age at onset:				
6–11 months ..	2	2	1	3
12–17 ,, ..	2	3	3	2
18–23 ,, ..	1	3	2	2
2–3 years ..	3	1	2	2
3–4 ,, ..	7	0	3	4
4–5 ,, ..	2	3	2	3
Total.. ..	17	12	13	16
Year of onset:				
1951	1	0	0	1
1952	3	3	2	4
1953	3	5	7	1
1954	0	1	0	1
1955	10	3	4	9
All years	17	12	13	16
Interval between vaccination and onset:				
Unknown ..	1	..	0	..
Less than 6 months ..	1	..	1	..
6–11 months ..	2	..	3	..
1–2 years ..	6	..	6	..
2–3 ,, ..	4	..	2	..
3–4 ,, ..	3	..	1	..
All intervals ..	17	..	13	..

required scale should be undertaken, and it would be particularly

interesting to compare areas of high and low poliomyelitis incidence (paralytic and non-paralytic separately), bringing in areas where the proportion of children vaccinated differs considerably (Ministry of Health 1954).

We are indebted to Dr. John Knowelden, of the Statistical Research Unit of the Medical Research Council, for advice in preparing this paper, and to Dr. J. A. Scott (medical officer of health for the County of London), Dr. Ian Taylor (principal medical officer, L.C.C.), and Mr. C. W. Shaddick (statistician, L.C.C.) for their interest.

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HYPOCALCÆMIA IN ACUTE PANCREATITIS

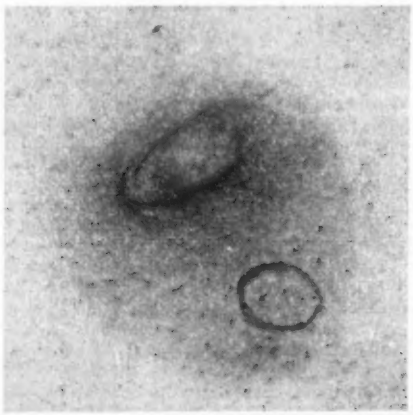
R. T. TURNER-WARWICK
M.A., B.Sc., B.M. Oxfd, F.R.C.S., M.R.C.P.
SENIOR SURGICAL REGISTRAR, MIDDLESEX HOSPITAL, LONDON

REDUCTION in the serum-calcium level is a recognised disturbance in acute pancreatitis. In the series of Edmondson and Berne (1944) a level below 7 mg. per 100 ml. indicated a fatal prognosis. The serum-calcium level in case 1 described here fell to 5 mg. per 100 ml. for several days before recovery, parenteral calcium therapy was required, and there was an interesting physical sign.

Case-reports

Case 1.—A man, aged 37, was admitted to Middlesex Hospital in July, 1954, with four days' history of constant epigastric pain, nausea, and vomiting. Jaundice had been present for two days. The pain did not radiate to the back (Taylor 1949). Up to this time the patient had been quite well except for three similar attacks in 1944, 1949, and 1950; each had been associated with jaundice, vomiting, and pain, and had lasted two or three weeks. Inflammation of the gall-bladder had been diagnosed, but a cholecystogram in 1949 was said to be normal.

On examination the patient was obese (17 stone), jaundiced (serum-bilirubin level 9 mg. per 100 ml.), and dehydrated. His temperature was 100·2°F and skin cold and sweaty. While his blood-pressure was being measured, a positive Trousseau's sign developed (serum-calcium level 6·5 mg. per 100 ml.). His abdomen was distended and generally tender, bowel sounds were not heard, and rebound tenderness was present. Naunyn's (Murphy's) sign was negative, and straight radiography of the abdomen showed a few fluid levels. Acute pancreatitis was diagnosed; the vomit and stomach aspirations (66 oz. in the first twenty-four hours) contained the altered blood not uncommonly seen in this condition. The serum-amylase level was 230 units (four days after the onset of symptoms), serum-potassium level 4·2 m.eq. per litre, serum-sodium level 136 m.eq. per litre, serum-chloride level 80 m.eq. per litre, serum-bicarbonate level 30 m.eq. per litre, blood-urea level 170 mg. per 100 ml., blood-sugar level 204 mg. per 100 ml., leucocytes 26,000 per c.mm. (polymorphs 87%, lymphocytes 7%, monocytes 6%).



Area of discoloration around umbilicus, with one area of fat-necrosis outlined.

Treatment and Progress.—Restorative electrolyte therapy and treatment with penicillin and streptomycin were started. On the second day after admission the patient's condition was deteriorating; he became confused and developed spontaneous carpopedal spasm (serum-calcium level 5·5 mg. per 100 ml., blood-urea level 220 mg. per 100 ml., no significant change in the serum-electrolyte levels). The tetany was relieved by 20 ml. of 10% calcium gluconate (200 mg. of calcium) given intravenously twice daily. Slight but definite discoloration developed around the umbilicus (Cullen's sign), and within this area two hard nodules ½ inch in diameter were felt in the subcutaneous tissue (see figure). There was a small umbilical hernia, and fat-necrosis seemed the likely cause of the nodules.

On the fourth day after admission the patient lapsed into coma. Trousseau's and Chvostek's signs became negative, although the serum-calcium level had fallen to 5 mg. per 100 ml. The serum-phosphate level was 6·5 mg. per 100 ml., serum-albumin level 3·1 g. per 100 ml., serum-globulin level 2·3 g. per 100 ml., serum-alkaline-phosphatase level 9 units, serum-magnesium level 4·2 mg. per 100 ml., serum-potassium level 4·0 m.eq. per litre, serum-sodium level 140 m.eq. per litre, serum-chloride level 85 m.eq. per litre, and serum-bicarbonate level 30 m.eq. per litre. The blood-urea level had risen to 270 mg. per 100 ml.; an oliguria of less than 10 oz. a day was present for the first three days, but thereafter the daily urinary output did not fall below 20 oz. Intravenous therapy was continued, and 20 ml. of 10% calcium gluconate was given twice daily.

On the sixth day the serum-calcium level was 5·2 mg. per 100 ml. and serum-phosphate level 9 mg. per 100 ml.; *on the seventh* the serum-calcium level was 6·7 mg. per 100 ml. *On the eighth* the level of consciousness rose appreciably after the intravenous injection of calcium, and this was observed after subsequent injections. The serum-calcium level at this time was 8·3 mg. per 100 ml., the alkali reserve 32 m.eq. per litre, and the blood-urea level 156 mg. per 100 ml. The urinary output of calcium was 28 mg. in twenty-four hours (total volume 2850 ml.).

During the next few days the patient gradually became rational, the bowel sounds returned, the blood-urea and serum-calcium levels returned to normal, and he made a slow recovery. For several days after his return to full consciousness he had severe intention tremor and nystagmus on lateral deviation. Weakness of the shoulder-girdles and right arm persisted for a fortnight, and numbness of the front of the thighs for several months. Possibly the cutaneous nerves to the thighs may have become involved in the inflammatory change around the fat necrosis along the retroperitoneal course of these nerves; alternatively, it may have been simple meralgia paræsthetica.

Two months after the acute attack cholecystography did not show the gall-bladder, but intravenous 'Biligrafin' showed a dilated common bile-duct and filling of the pancreatic duct. The patient's weight was reduced to 14 stone, and a cholecystectomy was performed by Mr. Vaughan Hudson in December, 1954. A considerable quantity of biliary gravel was removed from the common duct, after which a probe passed easily into the duodenum. There was some residual thickening in the pancreas, but there were no symptoms of dysfunction.

Pathology.—The nodules in the area of umbilical discoloration, one of which was ringed before the photograph was taken, did not change in size appreciably during the week after their appearance. The nodules were excised under local anæsthesia on the twelfth day of the attack. Histology showed an area of typical fat-necrosis, and the calcium content in this was 1000 mg. per 100 g. (wet weight) of tissue, compared with 15 mg. per 100 g. in the surrounding microscopically normal fat.

The term fat-necrosis was applied by Balser (1882) to the chalky lesions found in acute pancreatic necrosis. Langerhans (1890) showed that these were due to the action of the pancreatic lipase identified by Claude Bernard (1849) and were composed of calcium soaps. Quantitative calcium estimations were performed in

1944 (Edmondson and Berne). The deposition of calcium in the areas of fat-necrosis is certainly rapid.

Case 2.—A woman, aged 66, was admitted to Middlesex Hospital in September, 1955, with acute abdominal pain. The serum-amylase level was 1600 units and the serum-calcium level 8·5 mg. per 100 ml. She died within twenty-four hours of the onset of the attack, and at necropsy the greater omentum was found covered with a thin white layer of fat-necrosis. Shavings of this were taken with a razor to include as little of the underlying fat as possible. The calcium content of these was 840 mg. per 100 g. compared with 34 mg. per 100 g. in the underlying omental fat and 6 mg. per 100 g. in the subcutaneous fat; the ascitic fluid contained 7 mg. per 100 ml.

Comments

The process of fat-necrosis in acute pancreatitis clearly absorbs a considerable amount of calcium, estimated at several times the available circulating calcium during the first week in severe cases. A healthy person responds to a rapid loss of calcium by equally rapid mobilisation from the vast resources in the bones. The extent of this and the factors involved were discussed by Howard et al. (1953).

The patient with acute pancreatitis does not, however, maintain a normal serum-calcium level, a fact which may be helpful in the diagnosis because, although not a specific test, it persists longer than the serum-amylase level and is usually 8–9 mg. per 100 ml. A fall below 7 mg. per 100 ml. is very unusual in survivors and only occasionally seen in fatal cases.

The reasons for the unusually low serum-calcium level in case 1, and its slow response to intravenous calcium 400 mg. a day are unknown. The blood-electrolyte abnormality was otherwise relatively mild; the alkali reserve did not rise above 31 m.eq. per litre (69 vols. %), and the urinary output of calcium remained low. The disappearance of the tetany in the later stages, when the serum-calcium level was still 5 mg. per 100 ml., is likewise unexplained but may have been related to the decreasing level of consciousness.

Cullen's sign is more commonly seen in hæmoperitoneum and only occasionally in acute pancreatitis. Macroscopic areas of fat-necrosis in the subcutaneous tissues are very rare and presumably develop when lipase gains access to this tissue through a peritoneal herniation.

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ESTIMATION OF SERUM-AMYLASE

A SIMPLIFIED METHOD

S. SHALDON*
M.A., M.B. Camb.
LATE HOUSE-SURGEON, MIDDLESEX HOSPITAL, LONDON

THE value of serum-amylase estimation in the differential diagnosis of the acute abdomen is now well established (Burnett and Ness 1955). This communication describes a simple modification of Somogyi's (1938) method by which the test can be performed in the side-room of any surgical ward.

The incubating solution is kept at constant temperature by putting it in a 15 ml. test-tube which is inserted (through a central bore in the cork) into a vacuum flask filled with water at 37–40°C.

Besides the test-tube and flask, the requirements are: a thermometer; a stop-watch; four pipettes (one 10 ml., one 2 ml., and two 0·5 ml.); and two Pasteur droppers; a welled white tile; iodine (N/20); distilled water; and starch solutions.

Stock starch solution.—1·5 g. of starch is made into a paste with a few millilitres of cold water. This is poured into a solution of sodium chloride 5 g. in 80 ml. of boiling water. The mixture is then cooled and made up to 100 ml., and a few drops of chloroform are added as a preservative. Kept in a refrigerator, this solution will not deteriorate for at least 3 months.

Standard starch solution.—0·5 ml. of stock starch solution is diluted with 9·5 ml. of distilled water. 2 ml. then contains 1·5 mg. of starch. This solution must be freshly prepared.

Method

2 ml. of the standard starch solution is introduced into the test-tube placed in the vacuum flask, and is allowed to warm up for 3 minutes. 0·5 ml. of serum is then added and the stop-watch started. The solution is well mixed by sucking in and out of a Pasteur dropper, the dropper being left in the test-tube. At 1-minute intervals one drop of the mixture is withdrawn and added to a drop of N/20 iodine in the well of the porcelain tile. The colour of the reaction is noted, and the time (t) at which a blue colour is no longer visible is recorded. If the reaction takes place in less than a minute, the procedure is repeated with 0·1 ml. of serum and 0·4 ml. of distilled water to give a dilution of 1/5 of the serum.

The temperature of the fluid in the test-tube remains constant for at least an hour.

Calculation

A Somogyi unit of amylase is the amount that will destroy 1·5 mg. of starch in 8 minutes at 37°C (Somogyi 1938). Thus, since 1·5 mg. of starch is incubated with 0·5 ml. of serum, amylase activity in units per 100 ml. of serum $= \frac{8}{t} \times \frac{100}{0{\cdot}5} = \frac{1600}{t}$ where t is the time in minutes for the reaction to occur. If the diluted serum is used, the amylase activity must be multiplied by 5 for the actual level.

Results

Twenty normal sera were first tested by this method, and a range of 80–200 units per 100 ml. was established.

Thirty sera in cases of acute abdominal emergency were then tested. The highest amylase level was 1600 units per 100 ml. in a case of acute pancreatitis. Laboratory checks (Somogyi's 1938 method) of the raised levels showed a 10–20% difference compared with the simpler test. The test takes 20 minutes, from taking the blood, to demonstrate a serum-amylase level within the normal range. The incubation time is proportionately less when the level is higher.

The test has been adequately performed by untrained persons after a demonstration. The main difficulty lies in interpreting the end-point; but, if the amylase level is significantly raised, this presents no problem.

Summary

A simple modification of Somogyi's (1938) method of estimating serum-amylase is described. It is convenient for ward testing and can be applied by an untrained person. There is a 10–20% error compared with Somogyi's laboratory test.

I wish to thank Mr. J. H. L. Ferguson for his advice and encouragement, and Dr. E. T. Knudsen and Mr. E. Rose, of the Courtauld Institute of Biochemistry, Middlesex Hospital Medical School, for their kind coöperation.

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* Present address: Hammersmith Hospital and Postgraduate Medical School.

TORSION OF THE TESTIS

THREE ATYPICAL CASES

JOHN E. S. SCOTT
M.A., M.B. Camb., F.R.C.S.
SENIOR SURGICAL REGISTRAR, MIDDLESEX HOSPITAL, LONDON

THE diagnosis of torsion of the testis is notoriously difficult, and many cases are undoubtedly missed at the early stage when treatment may save the organ. I report here 3 atypical cases recently admitted to the Middlesex Hospital.

Case-reports

Case 1.—A boy, aged 16, awoke one morning to find that his right testis was swollen. He had some slight pain, which disappeared completely in about an hour and a half. Swelling persisted, however, and slowly increased for two days, when œdema of the scrotal and penile skin appeared. This latter alarmed him sufficiently to bring him to hospital, where examination showed considerable œdema and redness of the right side of the scrotum. The right testis was double its normal size and was hard and slightly tender. The epididymis could not be differentiated from the testis, and the cord was thickened. The absence of urinary symptoms and the fact that clinical tests showed a normal urine suggested torsion of the testis. A scrotal incision showed an intravaginal torsion of the testis, which, not being viable, was removed. The patient recovered without incident.

Case 2.—A boy, aged 13, slipped off the saddle of his bicycle and fell astride the crossbar two weeks before admission. Though he noticed nothing amiss at the time, he experienced pain in his right testis a week later. The pain increased and swelling appeared. Sulphonamides prescribed by his doctor did not effect any improvement, and by the end of another week the right side of the scrotum was red and œdematous and the penis also was swollen. The boy was then sent to hospital. He was not in much pain when he arrived, but his right testis was enlarged, hard, and tender, and the cord was thickened. The epididymis was impalpable. A traumatic hæmatocele with testicular hæmatoma was diagnosed. A scrotal incision showed intravaginal torsion of the testis, which, being gangrenous, was removed.

Case 3.—A boy, aged 18, was awoken one night by severe central abdominal pain, which moved rapidly to the right iliac fossa. He was seen in the casualty department of the hospital and admitted as a case of acute appendicitis. Further examination in the ward failed to show any signs in the abdomen, but the right testis and epididymis were found to be slightly enlarged and tender. They were in their normal position and the cord also was normal. Epididymitis was diagnosed although the ward urine test was normal. During the next two days the swelling and tenderness practically disappeared, but on the morning of the third day the swelling recurred, and œdema of the scrotal skin was found. The testis was enlarged, lying transversely in the upper part of the scrotum, and the cord was thick. The epididymis could not be differentiated from the testis. Torsion was diagnosed. When the patient was anæsthetised and prepared for operation, the testis was found to have become untwisted. It was exposed through a scrotal incision and was found completely infarcted. The cord was broad and flat and could be twisted through 90° in either direction. The testis was removed.

Follow-up.—This patient was seen later as an outpatient, and attention directed to his left testis, which seemed unduly mobile. He was readmitted to hospital for exploration. At operation the testis, the epididymis, and the lower part of the cord were found to be completely invested by a visceral layer of tunica vaginalis, and the testis and epididymis were separated by a broad mesorchium. Since it is these deformities which make torsion of the testis possible, the tunica vaginalis was resected, and the testis was fixed in the scrotum by two catgut sutures.

Discussion

Torsion of the testis is uncommon: Wheeler and Clark (1952) collected only 9 cases in 40,000 hospital admissions; Ewert and Hoffman (1944) collected 489 published cases; and 8 cases have been collected from the records of the Middlesex Hospital since 1948. The symptoms and signs are accurately described in surgical textbooks, and diagnosis should not present difficulty.

The occurrence of 3 atypical cases in quick succession suggested that this might be an important reason why early diagnosis is not achieved as often as might be hoped. 208 case-reports (in 108 articles in British and American journals), in which fully descended testes had twisted, were read. The diagnosis in these cases had been confirmed either by operation or by manual untwisting. In only 16 (7·7%) were the symptoms atypical, in that pain was either absent or very slight. Medical advice was sought by these patients because of testicular swelling, and the diagnosis was made in most of them only at operation. There must, however, be many more unreported cases in which no operation has been performed and the testis has atrophied without benefit of diagnosis.

Torsion of the testis, though uncommon, usually presents with the typical symptoms and signs described in the literature, and diagnosis depends primarily on an awareness of the condition.

I wish to thank Mr. J. H. L. Ferguson and Mr. R. S. Handley for permission to report the cases, which were admitted under their care.

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PUERPERAL TETANUS

TREATMENT WITH MUSCLE RELAXANTS AND BY ASSISTED RESPIRATION

A. MELVIN RAMSAY
M.A., M.D. Aberd.
PHYSICIAN, INFECTIOUS-DISEASES DEPARTMENT
E. M. FRANCE
M.B. Lond., F.F.A. R.C.S.
SENIOR REGISTRAR, ANÆSTHETIC DEPARTMENT
B. M. DEMPSEY
M.B. Lpool, F.F.A. R.C.S.
REGISTRAR, ANÆSTHETIC DEPARTMENT
ROYAL FREE HOSPITAL, LONDON

PUERPERAL tetanus is extremely rare. In the last thirty-one years at least 6000 cases of puerperal infection have been treated in the infectious-diseases department of this hospital, but the case reported here is the first one of puerperal tetanus.

Adams and Morton (1955) state that only 334 cases, of which 210 followed abortion, have been published. They consider that puerperal tetanus is not only the most dangerous puerperal infection but also probably the most dangerous form of all tetanus infection, and that, even with the latest methods of treatment, the case-mortality remains 75–100%.

Weinstein and Beacham (1941) gave the average mortality in 170 cases as 84%, but in their own series of 14 cases the mortality was only 57%; they attributed the decrease to the more widespread use of tetanus antitoxin.

Hübner and Freudenberg (1954) reviewed 1894 cases of tetanus with 930 deaths (49%); 39 of these had followed abortion, with 27 deaths (69%).

It is clear that the use of muscle-relaxant drugs, coupled with tracheotomy and assisted respiration, has brought about a considerable improvement in the prognosis of tetanus (Woolmer and Cates 1952, Honey et al. 1954, Lassen et al. 1954, Shackleton 1954). At least 7 cases treated in this way have already been described but the following case presents features which make it worth recording; without muscle-relaxant drugs and assisted respiration through a tracheotomy tube recovery would have been impossible.

Case-report

A housewife, aged 33, was admitted to the puerperal-sepsis unit of the Royal Free Hospital, on Nov. 22, 1955.

She had had a miscarriage on Nov. 15, and six days later she experienced pain in the neck, stiffness of the jaw, and difficulty in swallowing.

On admission risus sardonicus, masseteric spasm, and opisthotonos were present; respiratory movements were restricted, leading to slight cyanosis, and any movement provoked generalised spasms. *Clostridium tetani* was isolated from a cervical swab taken on admission and again from uterine curettings taken on Dec. 3. Inoculated mice developed tetanus and died, confirming the diagnosis of post-abortum tetanus.

Treatment.—Immediately on admission tetanus antitoxin 200,000 units was given intravenously, and muscle relaxation was induced three hours later with intravenous suxamethonium ('Scoline'). The relaxant was given as a 0·1% solution for the first seven days, but the strength was reduced during the last three days of its administration. The total dosage was 8·6 g. and at no time did the dose exceed 1 mg. a minute. Sedation was secured with amylobarbitone sodium given either intravenously or intramuscularly as the attendant anæsthetist thought necessary. A total of 4·5 g. of amylobarbitone sodium was given, most of it during the first four days; thereafter phenobarbitone sodium gr. 3 was given intramuscularly twice daily. In the first sixteen days penicillin 32·5 mega units was administered. An additional dose of tetanus antitoxin 30,000 units was given intramuscularly twelve hours before curettage of the uterus on Dec. 3.

Control of Airway.—Soon after the administration of suxamethonium was begun control of the airway became difficult; so a cuffed endotracheal tube was passed under general anæsthesia. Twenty-four hours later it became obvious that both control of the airway and sealing of the lower respiratory tract would be necessary for several days; so a low tracheotomy was done through the sixth tracheal ring, and a shortened cuffed endotracheal tube was inserted. During the first three days periods of manually assisted respiration were found necessary. For this purpose a mixture of nitrous oxide and oxygen, with to-and-fro absorption with a Waters canister, was used. On Nov. 25 the wire mesh of the filters on the Waters canister broke away from the metal rim, and soda lime was spilt into both the rebreathing bag and the connecting tube. These were emptied when the defect was discovered; nevertheless some soda lime was later found to have been blown into the bronchial tree. Respiration was then assisted as required with the aid of a Beaver mark II respirator giving a mixture of oxygen and air. On Nov. 26 increasingly severe spasms with pronounced intercostal recession made it essential to increase the amount of suxamethonium to 1000 mg. in twenty-four hours to ventilate the lungs adequately. With this mixture the tidal volume without assistance fell to about 150 ml., and it was therefore thought advisable to use the Beaver machine continuously. Positive-pressure respiration was continued until Dec. 3, eleven days after admission and twenty-four hours after the end of treatment with suxamethonium. During this time the Beaver machine had been set to give a tidal volume of 400–500 ml. at a rate of 16 a minute and a pressure of 15 cm. of water. The inspired gases were passed through a 'Radcliffe' humidifier.

Posture and Physiotherapy.—In view of the supreme importance of changing position to prevent the accumulation of secretions in any part of the lungs the patient was turned every half-hour, and, with each change of position, the chest was percussed to dislodge mucus, and the trachea was aspirated through the tracheotomy opening. To assist liquefaction of secretions 'Alevaire' (which contains a detergent, 0·125% superinone, in sterile alkaline solution) was given as an aerosol for five minutes every hour.

Complications.—In spite of these precautions radiography of the chest four days after admission showed collapse of the upper lobe of the left lung. Next day radiography showed complete collapse of the left lung. Bronchoscopy resulted in the aspiration of a granule of soda lime together with mucus, and partial re-expansion was effected. Two days later total collapse of the left lung recurred, and bronchoscopy showed considerable œdema of the bronchial mucosa with pronounced narrowing of the lumen. Three more granules of soda lime were aspirated from the left main bronchus in the next three days, and the lung then slowly re-expanded. The collapse was probably initiated by the soda lime, which may also have accounted for the intense œdema of the bronchial mucosa. The lung was found to be completely re-expanded three weeks later.

Feeding.—For the first forty-eight hours the patient was given nothing by mouth but received 500 ml. of physiological saline solution and 2 litres of 5% dextrose intravenously every twenty-four hours. Gastric feeding was then begun, and the patient received $1^1/_2$ litres of milk and 6 eggs with added sugar and salt daily. Intravenous fluid was thereupon reduced to $1^1/_2$ litres in twenty-four hours in the same proportions of saline solution and dextrose. Gastric feeding was discontinued on Dec. 7, when the patient could swallow normally.

Subsequent Progress.—Suxamethonium was discontinued on Dec. 2, ten days after admission. No further spasms occurred. Although the dose of suxamethonium never exceeded 1 mg. a minute and was less for three days before the drip was discontinued, weaning from the Beaver apparatus proved difficult. Positive-pressure respiration had to be maintained for twenty-four hours after the suxamethonium was stopped and intermittently during the following two nights. The reason for this period of prolonged respiratory depression was not clear. It could have resulted from either accumulation of succinyl monochcline (Collier and Macauley 1953) or production of a dual block at the myoneural junction due to the large amount of suxamethonium used (Churchill-Davidson 1955). In an attempt to distinguish between these two possible factors 'Tensilon' 10 mg. was given while the patient was anæsthetised for evacuation of the uterus on Dec. 3. There was no significant improvement in the volume of respiratory excursion. After recovery from the anæsthetic a further 10 mg. of tensilon was given intravenously. Measurements of the tidal volume showed a doubtful increase from 300 to 350 ml. This improvement was not maintained after a dose of 2·5 mg. of intramuscular neostigmine. These tests failed therefore to distinguish between these two possible causes. A metal tracheotomy tube was substituted for the cuffed endotracheal tube two days later. On Dec. 23 the tracheotomy wound was closed, and on Jan. 6, 1956, the patient was discharged home cured.

Discussion

The prognosis of tetanus is usually based on the length of the incubation period and the interval between the appearance of the first symptoms and generalised spasms, often called the "period of onset" (Cole 1953). If the incubation period is less than a week, or the period of onset less than forty-eight hours, the prognosis is regarded as poor. It is generally agreed that puerperal tetanus carries a particularly grave prognosis; in the present case an incubation period of six days and a period of onset lasting twenty-four hours added to the gravity of the outlook. Furthermore, splanchnic tetanus (Knott and Cole 1952), in which the muscles of deglutition and respiration are chiefly involved, practically always proves fatal. It can therefore confidently be claimed that the recovery of this patient could be attributed to the use of muscle-relaxant drugs combined with tracheotomy and assisted positive-pressure respiration.

Suxamethonium was chosen because of its short action which makes smooth control possible. Mephenesin was used by one of us (E. M. F.) in a previous case of tetanus with no respiratory embarrassment, and considerable difficulty due to venous thrombosis was encountered. Moreover, reports suggest that unless mephenesin is pushed to the point of producing hæmoglobinuria (Honey et al. 1954, Davison et al. 1949) it may not control spasms in severe cases. Tubocurarine and gallamine (Honey et al. 1954, Smith and Thorne 1952) have both been used with success, but their prolonged action makes control of dosage difficult. Also tubocurarine may lead to bronchospasm, and agranulocytosis and thrombocytopenia have been reported following its use (Gormsen 1955). Honey et al. (1954) report increased bronchial secretion after the administration of suxamethonium, but we did not observe it in the present case.

The Beaver mark II apparatus is convenient for prolonged assisted respiration, maintaining a constant tidal volume and pressure indefinitely, and eliminating such

hazards as blockage of the bronchial tree with soda lime.

Curettage of the uterus to eliminate the original focus of infection has usually been condemned as useless and possibly dangerous (Weinstein and Beacham 1941, Henderson and Johnson 1953). In the present case it was done safely and uneventfully; that it was necessary is confirmed by the isolation of *Cl. tetani* from the curettings, and that it was safe is shown by the fact that no untoward reaction developed.

Summary and Conclusions

Tetanus complicating abortion or pregnancy is rare and hitherto usually fatal (mortality over 75%); the first case seen in 6000 admissions to an infectious-diseases unit in thirty-one years is described.

The use of modern muscle-relaxant drugs in combination with assisted respiration, manual or mechanical, has greatly altered the outlook.

The uterus was emptied of placental remnants at a comparatively early stage for the same reason that early excision of necrosing muscle is practised.

A specialist team, including experienced nurses, such as is available at centres for the treatment of bulbospinal poliomyelitis, is essential to ensure success.

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TREATMENT OF SEVERE TETANUS
WITH *d*-TUBOCURARINE CHLORIDE AND INTERMITTENT POSITIVE-PRESSURE RESPIRATION

A. CRAMPTON SMITH
M.B. Edin., F.F.A. R.C.S.
ANÆSTHETIST, NUFFIELD DEPARTMENT OF ANÆSTHETICS AND RESPIRATION UNIT

E. E. HILL
M.B. Glasg., M.R.C.P.
REGISTRAR, PÆDIATRIC DEPARTMENT

J. A. HOPSON
B.M. Oxfd
HOUSE-PHYSICIAN

UNITED OXFORD HOSPITALS

INTERMITTENT positive-pressure respiration in association with some method of preventing spasm is an advance in the treatment of cases of severe tetanus (Lassen et al. 1954, 1956, Shackleton 1954). Four such cases have been treated in Oxford by pædiatricians and physicians in association with the respiration unit. There has been one death. The first case was reported by Honey et al. (1954). The present case was of exceptional severity and illustrates important points of treatment.

Case-report

On March 9, 1956, a boy, aged 7 years, was cut on the forehead by a sharpened stick used as an arrow. His doctor treated the wound, which was superficial, but gave no anti-tetanic serum, because of an allergic reaction to a dose of serum given eighteen months before. The wound became infected and was treated with intramuscular penicillin 500,000 units and oral aureomycin 250 mg. six-hourly.

On March 13 (fourth day after injury) the right side of the patient's face became stiff and trismus developed. On March 14 (fifth day after injury) he was admitted to Northampton General Hospital under Dr. H. Gosset, and that afternoon the first generalised tetanic spasm occurred.

Treatment

Oral and intravenous mephenesin modified the spasms, and the boy was given penicillin and intramuscular antitetanic serum in graded doses to a total of 75,000 units. He was nursed prone, and secretions thus tended to drain from his mouth. At 10 P.M., when he was seen by one of us, three or four generalised tetanic spasms were occurring each minute, which, though modified by mephenesin, were still severe enough to cause opisthotonos. He was anæsthetised with intravenous thiopentone, completely relaxed with curare, intubated through the mouth with a cuffed endotracheal tube, and transferred to the Churchill Hospital, Oxford, without incident, intermittent positive-pressure respiration being applied from an "Oxford" sucker inflator (Macintosh and Pratt 1939).

An elective tracheotomy was done at 3.30 A.M. on March 15 (sixth day after injury), and a short cuffed tracheal tube was substituted for the endotracheal tube. The source of intermittent positive-pressure respiration was at first a prototype Radcliffe respiration pump giving positive and negative pressure, which was later found to require modification, and was replaced by another prototype pump with mechanically operated valves but no negative-pressure phase. A humidifier was used throughout (Marshall and Spalding 1953).

It was decided to abolish the patient's tetanic spasms with intravenous curare, to sedate him with chloral hydrate in doses sufficient to prevent any later memory of his illness, and to give him promethazine to minimise allergic reactions. He was to have antibiotics, two-hourly postural changes, and physiotherapy to prevent chest complications, and was to be fed by gastric tube (Crampton Smith et al. 1954). Pulse-rate, blood-pressure, respiratory minute volume (expired air), pretracheal pressure, and pump-rate were to be recorded hourly. His chest was to be X-rayed daily, and biochemical estimations of his plasma-bicarbonate, blood-urea, plasma-sodium, plasma-potassium, and plasma-chloride levels were to be made frequently.

Twelve hours after this routine had been established, a further 40,000 units of antitetanic serum was given intravenously as a prophylactic measure, and the wound was excised.

Progress

The first day was satisfactory in that the patient's pulse-rate declined steadily from 160 to 130 and his blood-pressure remained about 120/170 mm. Hg. The respiratory minute volume was assessed by the Radford nomogram (Radford 1955), and the average volume used was 5 litres a minute. Curare was given in doses of 15 mg. intravenously through the tubing of an intravenous infusion, and later that day by intermittent injection through an indwelling Gordh needle. This dose paralysed the patient completely for about twenty to thirty minutes, and thereafter modified spasms became more and more apparent, at first as a myoclonic twitch of a limb and later as a jerky convulsive movement of the patient's whole body. Curare 315 mg. in twenty-four hours was necessary to control the spasms and chloral hydrate gr. 22 was given six-hourly.

On March 16 (second day of treatment) the patient's general condition deteriorated. The modified tetanic spasms, when not completely abolished by curare, became very numerous and required as much as 640 mg. of curare in twenty-four hours to control them (see figure). After successions of these modified spasms bradycardia occurred, and his blood-pressure was generally raised, being higher after spasms and after the short periods when he was disconnected from the respirator for tracheal suction. The patient's extremities became cold and cyanosed, and his appearance suggested peripheral vascular failure.

The positive-negative pressure pump in use was changed to one known to give very accurate records of respiratory minute volume but without a negative-pressure phase. The minute volume was increased to 6 litres a minute, and 100% oxygen was substituted for air. This was followed by improvement in the patient's colour and a fall in blood-pressure, but it was not until March 20 (sixth day of treatment) that there was a sustained fall in pulse-rate, with a definite improvement in his general condition.

During this period of grave illness, on March 18 (fourth day of treatment), his temperature rose to 104·8°F but fell rapidly after tepid sponging, and pyrexia did not recur.

On March 23 (ninth day of treatment) the plasma-bicarbonate level, which had risen over the previous four days, reached 25 m.eq. per litre (see figure). The respiratory minute volume was increased further to 8 litres a minute—a figure considerably in excess of that which would be expected for a child of this size.

Chest complications gave rise to little anxiety. The patient's secretions remained liquid and only slightly purulent. On March 21 (seventh day of treatment) the right upper lobe collapsed but was re-expanded by March 26, after the attention of the physiotherapists had been directed to it.

Between March 20 (sixth day of treatment) and March 29 (fifteenth day of treatment) there was very little change, except that on March 23 (ninth day of treatment), since the patient showed no signs of consciousness when the effect of curare was wearing off, the dose of chloral hydrate was reduced to gr. 11 six-hourly. From 300 to 500 mg. of curare was required in twenty-four hours to control the spasms, but the patient's general condition remained satisfactory.

On March 29 (fifteenth day of treatment) there was a fourteen-hour failure of electric current, and intermittent positive-pressure respiration was applied by hand until an emergency electricity supply was connected. This time was used to assess the progress of the tetanus, and curare was withheld for four hours. Tetanic spasms became severe as curarisation wore off, and bradycardia after spasm, which had occurred on the second day, was again observed. The patient's pulse-rate increased, and his blood-pressure became variable, with hypertension after spasms and after tracheal suction. In spite of the resumption of full doses of curare he did not completely recover from this incident for twenty-four hours.

On April 6 (twenty-third day of treatment) another attempt to discontinue the use of curare was made. It was anticipated that there would be a period during which the patient would be partially curarised and unable to ventilate himself adequately yet would have sufficient muscle power to oppose the inspiratory effort of the respirator. Rectal thiopentone 1 g. per 50 lb. of body-weight was given to cover this period of partial curarisation. When the thiopentone had taken effect, the child no longer made his usual efforts to breathe when disconnected from the respirator for tracheal suction or turning but, when stimulated, had a severe opisthotonic spasm —the first observed during the whole of his treatment. In addition an increase in pulse-rate and a fall in blood-pressure, together with cyanosed and cold extremities, suggested peripheral vascular failure, but on this occasion the resumption of full doses of curare quickly improved his condition.

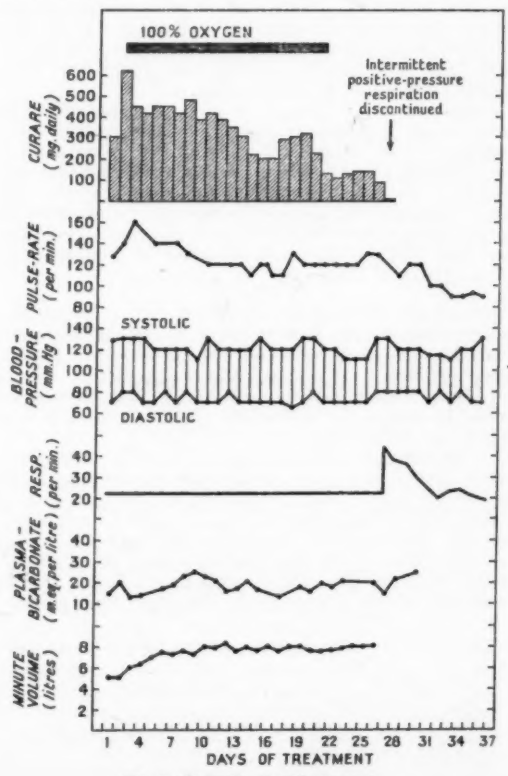

Chart of treatment and progress.

Curare was finally discontinued on April 9 (twenty-sixth day of treatment). The dosage over the final twenty-four hours was 90 mg. Four hours after the last dose of curare the patient started to breathe out of phase with the respirator and was disconnected from it. During the next two hours he was very restless but not clinically cyanosed, and then quite suddenly he fell asleep and gave no further indication of respiratory insufficiency.

The cuffed tracheal tube was left in position, a steam kettle kept the room humid, and he was encouraged to swallow. After a further twenty-four hours his swallowing was adequate, but he could not eat solids, because of trismus. Pulse and respiration rates fell to normal over the next week, and on April 12 (twenty-ninth day of treatment), swallowing being normal, a metal tracheotomy tube was inserted. This was removed (by the patient) on April 17 (thirty-fourth day of treatment). When muscle tone recovered, it became obvious that there was an abnormality of the right side of his face, at first thought to be residual local tetanus, but later diagnosed as a facial paresis. This condition improved slowly; and on May 7, just before discharge, he had only slight facial weakness and some trismus. He could run and play football. His behaviour, although he was intelligent (Binet-Simon tests showed a normal intelligence quotient), was rather aggressive and noisy. His schoolmaster, however, informs us that these traits were present before his illness, and his parents notice no change.

Discussion

d-Tubocurarine chloride was the relaxant chosen for use in this case for two reasons: (1) absolute muscle relaxation can always be obtained if enough curare is given; and (2) curare has been successfully used in other cases (Honey et al. 1954). In the present case the standard dose of curare was 15 mg. given intravenously, and this dose abolished all muscular movement for a time. Spasms, modified to myoclonic twitching, recurred after twenty to thirty minutes, and the nurse in charge of the patient gave more curare when these twitchings became obvious. The time interval varied slightly from nurse to nurse and depended also on the amount of stimulation. We formed the opinion that the occurrence of even these modified spasms adversely affected the patient's general condition, and we would probably be even more lavish with the dosage of curare in a future case. The total dose of curare used in the present case was 7640 mg., and the highest daily dose 640 mg.

For the first two twelve-hour periods of his treatment relaxants were administered through the tubing of an intravenous infusion. Thereafter curare was given through a Gordh needle by the nurse looking after the child. The position of this needle was changed at intervals of about twelve hours, and it was found that these frequent changes prevented venous thrombosis, and that veins could be used more than once if rested. In fact, only the small veins of hands and feet were used during his illness, and thrombosis occurred only in the veins used for the continuous infusions. Perhaps, if suitable veins for a Gordh needle are difficult to find, the relaxant of choice might be given by intramuscular or subcutaneous injection with hyaluronidase (McDonald and Bryce-Smith 1955, Mushin 1956).

Our impression was that curare was present in the body for several days after its administration had been discontinued. This was borne out by an increase of trismus for four days and by the presence in the urine of a curare-like substance seven days after the last dose had been given.

With full relaxation, sedation sufficient to obliterate any memory of the illness is all that is necessary, and chloral hydrate was chosen as having been commonly used over long periods. The dose at first used was gr. 22 six-hourly. It was reduced after nine days to gr. 11 six-hourly and again increased to gr. 22 six-hourly to cover the final reduction of curare. Attempts to assess the patient's level of consciousness were made difficult by his paralysis, but he has apparently no recollection of his illness from the time thiopentone was given before transporting him till intermittent positive-pressure respiration was discontinued. Hæmoglobin estimations and white-cell counts showed no significant variation from normal.

The respirator used at first was a prototype Radcliffe positive-negative-pressure respirator (Russell et al. 1956). This was changed at midday on the second day to a Radcliffe pump with mechanical valves but no negative-pressure phase. The inspiratory phase was a third of the respiratory cycle, and this pump worked very satisfactorily for the rest of the patient's illness. This change was made when his peripheral circulation was considerably depressed, and it did not have any deleterious effect. On the contrary, an increase of minute volume and the substitution of 100% oxygen for air improved his condition in spite of the absence of a negative-pressure phase. The minute volume was later increased again to 8 litres a minute in response to a rising plasma-bicarbonate level over four days (see figure).

The diet was based on an intake of 72 oz. of milk daily with additional glucose and 'Casilan' to provide 1750 calories. The high-protein diet usually given to these patients was not given, because this patient's blood-urea level never fell below 50 mg. per 100 ml., nor had it altered ten days after tube feeding had been discontinued—a finding that is being further investigated. His voracious appetite after normal feeding was resumed might suggest that this calorie intake was insufficient.

The urinary output was adequate, catheterisation was unnecessary, and his bowels were satisfactory regulated with liquid paraffin.

Penicillin and streptomycin were given for the first week against the causal organism and prophylactically against chest complications. Sulphadimidine in small doses was given for the rest of his illness and, in association with physiotherapy and changes of posture, controlled his chest infection. Promethazine was given to minimise allergic reactions.

Summary

A case of severe tetanus is described in which the incubation period was four days and the period of onset two days.

For twenty-six days the patient was treated with paralysing doses of curare (up to 640 mg. in twenty-four hours to a total dose of 7640 mg.) and respiration was maintained by intermittent positive pressure from a Radcliffe respiration pump.

Chloral hydrate was given to prevent any memory of the period.

The patient made a complete recovery.

We wish to thank Dr. Hugh Ellis, under whose care this patient was admitted, for permission to publish; Dr. W. Ritchie Russell for much helpful advice during the management of the case and in the preparation of this paper; the sister and nurses of the pædiatric ward of the Churchill Hospital, Oxford, without whose intelligent application this patient could not have survived; and Messrs. Burroughs Wellcome for estimating curare in the urine.

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TWO SIMPLE TESTS TO DETECT OMISSION OF PRESCRIBED PARA-AMINOSALICYLIC ACID

H. G. PENMAN
M.A., M.B. Camb., M.R.C.P.
ASSISTANT LECTURER IN CLINICAL PATHOLOGY

D. G. WRAITH
M.A., M.D. Camb., M.R.C.P.
SENIOR MEDICAL REGISTRAR, DEPARTMENT OF THORACIC MEDICINE

ST. THOMAS'S HOSPITAL, LONDON

Ehrlich's reagent forms an orange or lemon-yellow compound with *p*-aminosalicylic acid (P.A.S.) and its salts and has been used for detecting and estimating this drug; it also gives a pink colour with urobilinogen.

Some difficulty might therefore have been expected when specimens of urine from tuberculous outpatients, many on P.A.S., were tested for urobilinogen as part of an investigation of liver function; but interference from the yellow P.A.S. compound seemed surprisingly infrequent. This finding prompted an investigation into the reliability of Ehrlich's test applied to urinary P.A.S. in patients known fairly certainly to be taking this drug. Early-morning specimens of urine from 22 tuberculous inpatients, 8 of whom were on P.A.S. 12–20 g. a day, were tested. In 7 of the 8 P.A.S. cases there was a definite colour reaction, but none was seen in the 8th or in the 14 others not taking P.A.S. It was later discovered that the P.A.S. given to the patient whose urine gave the one unexpected result was being thrown away.

Several specimens of urine from outpatients supposed to be taking P.A.S. showed no trace of the drug. When subjected to the two tests described below, only 9 out of a random selection of 14 gave positive results. When questioned about this, some of the patients admitted that, for various reasons—e.g., gastric upset—they had temporarily omitted the drug, but others persistently denied having done so.

Long-term P.A.S. therapy is now often prescribed for tuberculous outpatients in combination with either isoniazid or streptomycin. It is clearly important that the P.A.S. be actually taken, because tubercle bacilli may otherwise quickly become resistant to one of the other drugs administered alone. We therefore draw attention to two simple tests to detect P.A.S. in urine. These tests are based on the reactions described by Venkataraman et al. (1948).

First Test

If 0·5 ml. of Ehrlich's reagent (0·7 g. of *p*-dimethylaminobenzaldehyde in a mixture of 150 ml. of concentrated hydrochloric acid and 100 ml. of water) is added drop by drop to 5 ml. of urine, P.A.S. can be detected by the immediate development of a lemon-yellow colour, with an orange or yellow precipitate if there is much P.A.S. (i.e., about 1%).

With sodium P.A.S. made up in water, a concentration of 1 : 50,000 can just be detected in this way; but, since the colour produced is not unlike that of urine, a urinary concentration of even 1 : 5000 is not easy to detect. Further, in vivo, some of the P.A.S. may be acetylated on the N atom and not react. In practice we found that, if the patient had his P.A.S. the previous evening, it was detectable in the first urine passed in

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the morning but might not be in the second, unless the morning P.A.S. had already been given.

The colour reaction depends on the free aromatic-NH_2 group, and sulphonamides react in the same way as P.A.S. Apart from this group of drugs there appear to be no substances with similar properties that are at all likely to be found in the urine. The reaction between Ehrlich's reagent and urobilinogen has already been mentioned.

Second Test

If 5% ferric chloride in 1% hydrochloric acid is added drop by drop to urine containing P.A.S., a deep reddish-brown colour will develop almost immediately. In any urine a light-brown precipitate may develop, and the ferric chloride should continue to be added until further drops produce no more change.

A concentration of 1 : 50,000 of sodium P.A.S. in water is readily detected, and the colour is quite unlike that of urine. P.A.S. acetylated at the –OH position will not react, but we found that, even if no P.A.S. had been taken on the morning of the test, the second specimen of urine showed a good reaction derived from the previous evening's P.A.S. The reaction becomes negative from twelve to twenty-four hours after a single dose; hence the urine of a patient taking P.A.S. four times a day should be continuously strongly positive in this test. The sodium and calcium salts behave similarly.

This reaction is, of course, less specific than that with Ehrlich's reagent, the same colour being given by urine from patients taking salicylates or aspirin, or in ketosis. A negative result, however, seems reliable.

Conclusion

We suggest that, if one or both of these tests are occasionally used in chest clinics, underhand perhaps though they may seem, some interesting results will be forthcoming.

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ADRENOCORTICAL TUMOUR WITH HYPOKALÆMIA AND FLACCID MUSCLE PARALYSIS

C. H. CAMPBELL
M.B. Sydney, M.R.A.C.P.
REGISTRAR IN MEDICINE

N. NICOLAIDES
M.B. Queensland
RESIDENT IN PATHOLOGY

A. W. STEINBECK
M.D. Sydney, Ph.D., M.R.C.P. Lond., M.R.A.C.P.
PHYSICIAN AND LECTURER IN MEDICINE

BRISBANE HOSPITAL, QUEENSLAND, AUSTRALIA

Conn (1955a) has drawn attention to a clinical syndrome due to the excessive secretion of the mineralocorticoid, aldosterone, as the result of primary adrenocortical disease, either hyperplasia or a tumour. In this syndrome of primary aldosteronism there are a loss of potassium from the body, an increase of body sodium, and a metabolic alkalosis. There is also nephropathy from the potassium depletion. Clinical features include recurrent and severe muscular weakness, progressing at times to transient paralysis, excessive thirst, paræsthesiæ, episodes of tetany, large volumes of urine, and hypertension.

After the initial description of the syndrome at least 15 cases have been recognised (Conn 1955b, Evans and Milne 1955, Foye and Feichtmeir 1955, Mader and Iseri 1955, Chalmers et al. 1956, Conn and Louis 1956). Of these cases 3 have been diagnosed in retrospect, 10 have been cured by removal of an adrenocortical tumour, and 1 has been cured by total adrenalectomy, and 1 proved fatal from metastases.

The following case, which is referred to by Conn and Louis (1956), is reported as another probable example of primary aldosteronism.

Case-report

A housewife, aged 39, was admitted to hospital on Aug. 2, 1955. At midday on Aug. 1 she had become intensely tired and gone to bed; her calf muscles seemed weak, and later that day she could not get out of bed without assistance. On admission she could not walk, and her legs felt decidedly heavy. She had previously been subject to episodes of muscle weakness which had passed away after one or two days.

Previous History

Since childhood she had had recurrent attacks of "pyelitis." Her first hospital attendance was in January, 1953, when she complained of severe occipital headaches and of the necessity to pass her urine frequently—symptoms that had been present for several years. She was six weeks pregnant and in her fifth pregnancy. Her blood-pressure was 210/110 mm. Hg. Her urine contained no protein and its specific gravity fell to 1·005 after a water load and only rose to 1·010 after restriction of fluids. Her blood-urea level was 28 mg. per 100 ml. Her pregnancy was allowed to continue: her blood-pressure remained high throughout, and she had a small antepartum hæmorrhage in the 27th week and mild proteinuria in the 37th week. Delivery was by cæsarean section in the 38th week. In October, 1953, the patient experienced a feeling of weakness and soreness in the shoulder muscles and, at the same time, had difficulty in sitting up, holding her head up, and lifting it off the pillows. In November, 1953, when there had been no vomiting or diarrhœa, unexplained weakness of the arms and legs, with difficulty in walking, occurred and lasted six days. On examination at that time she had doubtful weakness of the muscles of the trunk and arms and actual unsteadiness while standing. After a period of observation in hospital the condition was regarded as an anxiety state. By November, 1954, her main complaint was of recurrent "turns" since the last pregnancy. These consisted of pains in the back of the neck and shoulders, numbness of the left arm, loss of appetite, giddiness, and "an inability to do anything." She still had to void urine three or four times a night. Hæmoglobin was 10·3 g. per 100 ml., blood-urea level was 44 mg. per 100 ml., and an intravenous pyelogram showed poor excretion of dye but normal renal outlines. Throughout these attendances the patient's blood-pressure varied from 170/80 to 230/140 mm. Hg; the specific gravity of her urine was below 1·014 and the urine was usually protein-free, had normal centrifuged deposits, and was sterile on culture. During the early part of 1955 there were several episodes of diarrhœa lasting one or two days, but for eleven days before admission there had been no vomiting or diarrhœa.

Examination

The patient was listless and sallow-complexioned and had bilateral ptosis and a very dry skin; pulse-rate 90; blood-pressure 220/120 mm. Hg; apex-beat impalpable; and heart sounds normal. Apart from the ptosis, the muscles supplied by the cranial nerves were unaffected. There was bilateral foot-drop; the patient could not lift her head off the pillow, sit up, or raise her legs from the bed; muscle tone was decreased in the lower limbs; muscle weakness was generalised but worst in the anterior crural and anterior tibial groups of muscles; the plantar flexors of the ankle-joint were relatively strong; the muscles of the arms were much less weak than those of the legs. Most of the deep reflexes were absent, but the biceps and knee jerks on the right side and triceps-jerks on the left could be elicited; the plantar reflexes were flexor, but the abdominal reflexes were absent. Sensation was intact. The abdomen was not obviously distended, and bowel sounds were present. There was no œdema. The urine (sp. gr. 1·001) did not contain protein. Flaccid muscle paralysis due to hypokalæmia, as the result of potassium-losing nephritis, was diagnosed provisionally.

Investigations

A blood-count showed Hb 14·1 g. per 100 ml.; white cells 19,000 per c.mm. (neutrophils 89%). Serum-electrolyte levels: potassium 2·0, sodium 154·4, chloride 96·6, bicarbonate 26·2

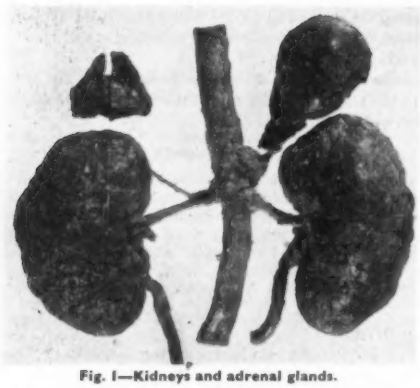

Fig. 1—Kidneys and adrenal glands.

m.eq. per litre; serum-calcium 11·3 mg. per 100 ml., and blood-urea 62 mg. per 100 ml. Electrocardiography showed horizontal heart, left axis-deviation; sinus rhythm with a normal P-R interval; depression and sagging of ST segment in leads I, II, aVL, aVF, and V_2–V_6; inverted T and prominent U waves in leads I, aVL and V_6; fusion of T, U, and following P waves in leads V_2–V_4; fusion of T and U waves in leads II, aVF and V_6—patterns associated with hypokalæmia (Surawicz and Lepeschkin 1953, Bellet 1955, Lepeschkin 1955).

Progress

The patient's general condition was essentially unaltered on the day after admission, but she was vomiting. An intravenous infusion containing potassium chloride was started. She died suddenly eight hours later without significant alteration in her general condition.

Necropsy Findings

The left adrenal gland, after fixation in formol saline solution, weighed 46 g. This mass was mostly due to an ovoid tumour measuring about 5·0 × 4·0 × 3·5 cm., and only a small piece of tissue at the lower pole resembled normal adrenal gland. The tumour was yellowish-brown, there were numerous blood-vessels on its surface, and on section it was vascular and divided into three areas: the one nearest the adrenal remnant was yellowish; another was bloodstained; and between these there was an opaque white zone (figs. 1 and 2). The right adrenal gland weighed 5 g. The right kidney weighed 134 g. and the left 148 g., and there were some depressed scars on their surfaces (fig. 1). The heart weighed 340 g., the greatest thickness of the left ventricular wall was 2 cm., and there was minor coronary atherosclerosis.

Histology

The adrenal tumour appeared to have arisen from the zona fasciculata. In the adrenal remnant there was no zonal atrophy (assessed on the width of the zones and cell size). The opaque white area of the tumour was a portion that had undergone degeneration. Hæmorrhage into the degenerate tumour caused the bloodstained appearances of the remainder. Individual tumour cells varied greatly in their size and shape, and some of them were arranged in cords; nuclear size was variable. The nuclei did not stain uniformly, nor did the cytoplasm. The commonest cell was large, with a small nucleus, and, in hæmatoxylin and eosin preparations, the nucleus was darkly stained and the cytoplasm pale, faintly eosinophilic, and "foamy" (fig. 3). The histological appearances were essentially those of an adrenocortical adenoma which was not uniformly well differentiated, particularly in some areas. Metastases had not been noted at necropsy. The right adrenal gland appeared normal. In Sudan-IV preparations the zona glomerulosa of the left gland was almost free from sudanophilic droplets. In the zona fasciculata the cells contained many large sudanophilic droplets, which distended them, and some birefringent material. The more superficial cells of the zona reticularis also contained sudanophilic droplets. The same appearances were found in the right adrenal gland. In the kidneys there were hypertensive changes in the blood-vessels but no fibrinoid necrosis; some of the glomeruli were hyalinised, and there was scattered infiltration of the cortices by lymphocytes. In most of the cells of the proximal convoluted tubules the cytoplasm was very vacuolar and the nuclei were against the basement membrane. The cytoplasm did not take up lipid stains, and

Fig. 2—Adrenocortical tumour, sectioned.

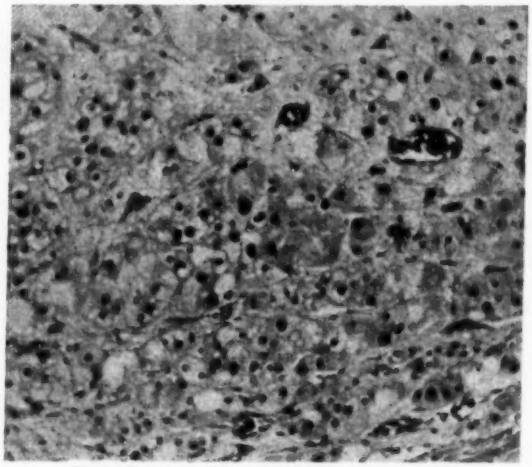

Fig. 3—Tumour. (Hæmatoxylin and eosin. × 150.)

the appearances were those associated with chronic hypokalæmia (Perkins et al. 1950, Keye 1952). In the heart there were scattered areas of hæmorrhage and cellular infiltration, mostly with polymorphs, in the subendocardial layers. Muscle-fibres near these areas were degenerate. Sections from a rectus abdominis muscle were not definitely abnormal.

Discussion

The clinical features of this case included hypertension, abnormal sensations and unexplained pains, fatigue, intermittent muscle weakness, and, finally, an episode of flaccid paralysis. The volumes of urine were large; the urine had a low specific gravity and was usually protein-free. There were no recognisable episodes of tetany, and in the final illness the serum bicarbonate levels were normal. On the whole, the clinical picture and findings are similar to those of primary aldosteronism.

Clinically, causes for a low serum-potassium level and for flaccid paralysis, other than potassium-losing nephritis, could be excluded. Earlier diagnoses in this patient had always included chronic pyelonephritis because she claimed a history of, and treatment for, recurrent attacks of "pyelitis" since childhood. However, when she was admitted for an attack of "pyelitis," her urine did not contain pus cells or organisms, and on several occasions

centrifuged deposits of the urine were normal and sterile on culture.

The features of primary aldosteronism are similar to those of potassium-losing nephritis (Brown et al. 1944). In the present case there was no definite histological evidence of either chronic pyelonephritis or nephritis, but there were the tubular lesions of hypokalæmia and some hypertensive vascular changes. Therefore it seems reasonable to regard this case as an instance of primary aldosteronism due to an adrenocortical tumour.

The tumour appeared to have arisen from the zona fasciculata. There was no convincing thinning of this zone either in the adrenal remnant or in the opposite gland, as reported by Conn (1955b), but its cells were distended by large sudanophilic droplets and contained birefringent material. Similar appearances were described by Chalmers et al. (1956), who, like Conn, found atrophy of the zona fasciculata. The zona glomerulosa in the present case and in that of Chalmers et al. contained scanty sudanophilic droplets; in neither case was birefringent material present. The significance of these findings is not clear (Stoner et al. 1953, Greep 1954, Landing 1955, Symington et al. 1955, Yoffey 1955). Previous tumours have been essentially well-differentiated cortical adenomata, but the present one was not, particularly in some areas. Foye and Feichtmeir (1955) reported a case of Conn's syndrome with recurrence after operation in association with metastases. It is therefore unlikely that a causal tumour will always be benign.

On occasions hypertension was considerable in the present case, but its relationship to the tumour is unknown; Mader and Iseri (1955) accept one for their case, and Chalmers et al. (1956) suggest that a "salt plethora" was a factor in their patient.

An excessive secretion of aldosterone can only be assumed in the present case. Sayers et al. (1955) prefer to await further data before assessing the significance of a suggested increase in the urinary excretion of aldosterone in their patient, and Chalmers et al. (1956) found only a small increase in theirs. Aldosterone was not detected in the plasma of another case (Garrod 1955), and presumably a considerable secretion would have been. Analysis of the tumour in one case (Mader and Iseri 1955) revealed significant quantities of corticosterone as well as aldosterone, and the urine in another case contained excessive amounts of 17-ketogenic steroids in addition to aldosterone (Foye and Feichtmeir 1955). Perhaps, then, steroid excretion in this syndrome will prove more variable than expected, and found at first (Conn 1955a and b), although hyperaldosteronism is the basic abnormality.

Summary

A patient with recurrent muscle weakness and final flaccid paralysis due to excessive loss of potassium is described.

Hypertension was present, and urinary concentrating power was impaired.

At necropsy a tumour of the left adrenal cortex was found.

We are indebted to Dr. V. E. Sampson, under whose care the patient was, for permission to report this case, and to Prof. J. H. Tyrer for his encouragement.

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CAT-SCRATCH FEVER

REACTIVATION BY INTRADERMAL TEST

RAE LL. LYON
M.B. Edin., M.R.C.P.E.
SENIOR MEDICAL REGISTRAR, ROYAL NORTHERN INFIRMARY AND RAIGMORE HOSPITAL, INVERNESS

THE recognition of a specific clinical picture following the scratch or bite of a cat was the result of work carried out independently by Foshay in the United States and Debré in France, who found that the cat's marks often persisted, to be followed later by pyrexia, generalised systemic reactions, and enlargement of regional lymph-nodes, which tended to break down and to discharge a sterile pus, but without lymphangitis appearing. Rose's intradermal test for cat-scratch fever contributed to the establishment of this recognisable disease as an entity (Daniels and MacMurray 1954).

Cat-scratch fever has been extensively studied in America, particularly by Daniels and MacMurray (1954), and on the Continent by Mollaret et al. (1951), who have collected large numbers of cases, and there can be little doubt that cat-scratch fever may be encountered throughout the whole world. Reports in Britain include a very full review by Brand and Finkel (1956), and the 8 cases which have been described are all from the southern part of the country (Wigley 1952, Garai 1952, Campbell and Wheaton 1952, Cox 1952, Bettley and Fairburn 1953, Brand and Finkel 1956).

Since cat-scratch fever is more likely to affect young people, the differential diagnosis is important. The case reported here extends the distribution in Britain because it was observed near Inverness. It also presented some unusual features.

Case-report

A well-developed girl, aged 16, was admitted with pyrexia and pains in the limbs and joints and was provisionally diagnosed as having rheumatic fever.

On examination no significant abnormality was detected; in particular, there was no enlargement of the spleen, lymphadenopathy, or joint swelling. Movements of the limbs were free and full. The patient felt her right arm particularly uncomfortable; part of her right index finger was indurated and bluish-red, and small puncture marks were still clearly visible in the centre of this discoloured area. She had been bitten on this finger by a cat about a month previously. Her temperature was 100°F and pulse-rate 90. Her pyrexia, which lasted ten days before settling completely, varied between 99°F and 103°F and was not influenced by salicylates.

Four days after admission movement of her right shoulder became very painful, and an enlarged tender gland could be felt high up in the axilla, but no lymphangitis was ever demonstrated. From the time of development of the lymphadenopathy varied rashes appeared, changing in character with surprising speed. The most prominent was a plum-red morbilliform rash, which affected generally the right arm and face, disappeared in a few hours, and recurred equally quickly. Typical erythema nodosum and erythema marginatum were also seen on the upper limbs and trunk. The pyrexia disappeared spontaneously, and a few days later the rashes and axillary adenitis were also gone.

Investigations.—Examination of the blood showed hæmoglobin 94%; white cells 5100 per c.mm. (polymorphs 62%, lymphocytes 25%, monocytes 12%, eosinophils 1%). On

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admission the erythrocyte-sedimentation rate was 19 mm. in the first hour (Wintrobe), rising by the fifth day to 51 mm. in the first hour and thereafter gradually dropping to normal. Microscopy showed no abnormal urinary constituents, but there was slight albuminuria, which lasted only a few days. Radiography of the chest and bones showed no abnormality. A blood-culture was sterile. A Mantoux test 1 : 10,000 was negative. The anti-streptolysin titre was insignificant. Agglutination tests for typhoid, paratyphoid, other salmonellæ, and *Brucella abortus* were all negative. The complement-fixation test for the psittacosis/lymphogranuloma-venereum group of viruses was also negative.

On the eighteenth day after admission, when the patient clinically appeared completely back to normal, 0·1 ml. of cat-scratch-fever antigen (Colindale) was injected intradermally into the left forearm. No local reaction was noted, but the painful swelling of the glands in the right axilla recurred, along with the pyrexia and a recrudescence of the rashes. This induced illness continued for a fortnight without showing any signs of improvement. When the patient's temperature had slowly climbed to 104°F oxytetracycline was administered. Within forty-eight hours her temperature was normal and she was feeling much better. In a week the rash and swelling disappeared. Uninterrupted convalescence followed, and the patient remains well.

The Cat

It was impossible to identify the assailant in this attack from among a family of a cat and her three kittens. One kitten, which was too small to be responsible for the scratch, had been killed shortly after by the owner because it appeared to be diseased. About four months after the patient had been scratched, when the cat and her remaining two kittens were studied locally at the College of Agriculture veterinary laboratory, one of the kittens was observed to be sneezing and was not thriving. Subsequently the other two developed this upper respiratory infection before they were all destroyed. The post-mortem appearances suggested that this was due to a virus infection, the strongest-looking kitten having in addition a small patch of pneumonitis.

Discussion

The diagnosis in this case was based on a very typical sequence of events, appearances, and laboratory data. The rash appeared to be toxic, associated with the infection and not with the salicylates. The self-limiting nature of cat-scratch fever is illustrated by the apparent recovery after ten days. A particularly striking feature was the way in which the entire sequence was repeated after the intradermal test in spite of the fact that there was no local effect from the antigen. It has since been ascertained that no other case, tested with this batch of antigen, behaved in this manner.

The antigen is a relatively crude product made from pus from the suppurating gland of an infected patient, and uniform results need not necessarily be expected. Daniels and MacMurray (1954) are among those who recognise that the typical clinical picture may present a negative skin-test. Gifford (1955) has observed in some cases a delay before a positive reaction appears and in others a small granuloma persisting at the site of injection.

I have been unable to trace any published case in which, after the skin test, there was a gross systemic reaction as in this girl.

It is generally agreed that a virus, probably of the psittacosis/lymphogranuloma-venereum group, is responsible for this infection, and that, though contact with a cat is common, there may be no such history. Several workers have tried to demonstrate the infection in cats. As Gifford (1955) points out, the feline pneumonitis of Baker was suspect for a while, but he and others have shown that the cats involved are often robust and no infection from them can be passed on to mice. Gledhill (1952) demonstrated a second virus infection of the respiratory tract in cats which, unlike feline pneumonitis, could not be transmitted to mice. More detailed studies of the cats will therefore be required before they can be exonerated from being the source of the infection.

Summary

A case of cat-scratch fever from Northern Scotland is described in which the intradermal injection of antigen renewed the features of the general infection.

Four months after biting the patient, the family of cats which were responsible all showed a virus infection of the upper respiratory tract, and one had pneumonitis.

I wish to thank Dr. J. Ronald, consultant physician, for his ready advice and for permission to publish this case; Dr. H. Williams, bacteriologist, for his willing help; and Mr. G. A. M. Sharman, M.R.C.V.S., for investigating the cats.

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Preliminary Communication

CHEMICAL ESTIMATION OF ALDOSTERONE IN URINE

THE recognition of aldosterone as the main mineralocorticoid has led to much interesting speculation about the factors which regulate its secretion by the adrenals. At the same time, the discovery of pathological conditions caused by overproduction of aldosterone makes a practical and reasonably accurate method of assaying aldosterone highly desirable. Such a method has recently been developed in our laboratory, and the procedure is as follows:

Half of a 24-hour sample of urine is hydrolysed at pH 1 at room-temperature for 24 hours and continuously extracted with five successive portions of chloroform. The chloroform fractions are then washed with 5% sodium-carbonate solution and water and dried in vacuo. The residue is further purified by a partition between toluene-ligroin and methanol-water (5 : 5 : 7 : 3), and the residue of the methanol layer is subjected to paper chromatography using a toluene-octanol-methanol-water (98–2–50–50) system. (In this system aldosterone moves between cortisone and cortisol and separates well in 4 hours.) After elution the aldosterone fraction is chromatographed in a Bush system, which separates aldosterone from a substance that can be shown to interfere with the final colorimetric estimation.

For determining the purified aldosterone we use a modification of the reaction of Gornall.[1] The 2·4 dinitrophenylhydrazone of aldosterone is formed at 100°C with the 2·4 dinitrophenylhydrazine reagent. The hydrazone precipitate is fixed with benzoic acid and then washed three times with a saturated solution of benzoic acid in dilute sulphuric acid.

The final precipitate is dissolved in 50% ethanol. After addition of a pellet of solid sodium hydroxide, the extinction curve of the solution is measured in a Beckman spectrophotometer against an identically treated blank. In this way the characteristic 2·4 dinitrohydrazone curve of aldosterone is obtained.

Calculated against a standard,[2] 5–17 μg. of aldosterone was found in the 24-hour urine of twelve normal subjects. The mean value is about 10 μg. per 24 hours. Details of the method will be published elsewhere.

Department of Clinical Endocrinology and Diseases of Metabolism, University of Leyden, Holland

A. J. MOOLENAAR
D.Sc. Leyden

1. Gornall, A., MacDonald, M. P. *J. biol. Chem.* 1953, **201**, 279.
2. Kindly supplied by Dr. H. L. Mason and Messrs. Organon N.V., Holland.

New Inventions

DRAINAGE APPARATUS FOR USE AFTER PROSTATECTOMY

THE apparatus illustrated here is intended for routine use after all forms of prostatectomy. It provides a simple means of making sure that the patient's catheter is draining continuously and it minimises the risk of infection attendant on the use of indwelling catheters.

The importance of closed drainage is widely recognised, and it can be achieved with many different patterns of bottle; but the design of none of these takes account of the equally important need to maintain the drainage continuously and without obstruction.

At present, unless continuous irrigation (almost universally condemned) is adopted, there are two commonly used methods of testing the continuity of the drainage.

1. The nurse examines the glass connection between the catheter and the drainage tubing, and from its contents guesses whether the catheter is blocked. This is clearly an inaccurate method, and it leads to many a blocked catheter being regarded as patent and to the frequent syringing of patent catheters thought to be blocked. This last procedure is a potent source of infection and should only be undertaken when absolutely necessary.

2. The nurse changes the drainage bottle every half-hour. This method shows clearly how much has drained in that time; but it is laborious and time-consuming and hence tends to be neglected, and it has the added disadvantage that the drainage can hardly be regarded as closed.

Our apparatus consists of a large glass jar (fig. 1A) with a small one (B) fixed within its metal lid. The lid is provided with a rubber washer and makes an airtight fit on the large jar. In the base of the small jar is a hole, half an inch in diameter, which is closed by a rubber washer on the end of a spring-loaded plunger (C).

Urine and blood drain via the catheter and the usual length of rubber tubing into the small jar, and by pressing the plunger the nurse can see the contents of the small jar empty into the large one. If this is done half-hourly, definite visual evidence is provided of the continuity of the patient's drainage. If the catheter has become blocked, the small jar will of course be empty and pressing the plunger will yield no result: steps can be taken promptly (and justifiably) to unblock the catheter. If, on the other hand, the amount of fluid drained exceeds the capacity of the small jar, the excess can overflow through a hole in its side (fig. 1 arrows). Once drainage has been satisfactorily established and blood is disappearing from the urine, the plunger need no longer be operated, and the contents of the small jar can be left to overflow continuously into the large jar.

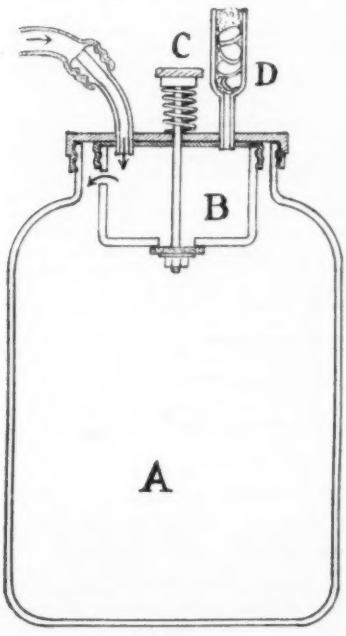

Fig. 1.

The air-vent (D) has been designed to take formaldehyde tablets wrapped in gauze, and 4 oz. of 10% solution of formaldehyde is placed in the large jar during use, on the principles advocated by Riches.[1]

During use the large jars are changed as necessary, and after thorough cleansing are sterilised in a 1 in 2000 solution of 'Hibitane' (bis-*p*-chlorophenyldiguanidohexane acetate). Their generous capacity of 80 fluid oz. makes this a reasonably infrequent procedure, and the fact that they are graduated in ounces enables the urinary output to be recorded accurately and simply.

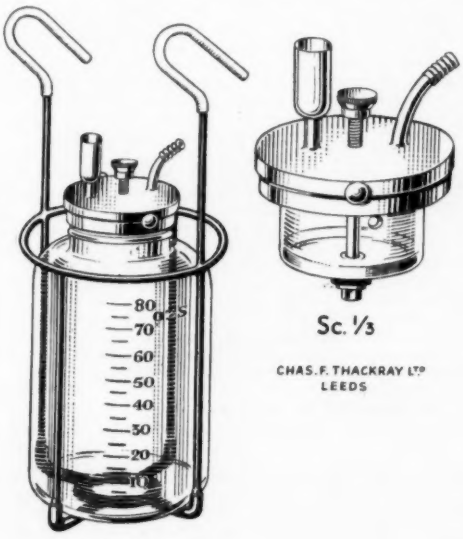

Fig. 2.

The complete assembly of the metal lid, plunger, and small jar (fig. 2) can be taken to pieces for cleaning and is then reassembled and autoclaved before use. When not in use the large jar is stored with formaldehyde tablets in it, the top being sealed with a plain lid and adhesive tape.

It is necessary to have a special cradle to attach the apparatus to the bed rail, and fig. 2 shows one which has been made in the hospital workshop.

We have used the drainage apparatus in this hospital for more than a year and have found it extremely satisfactory; it undoubtedly gives much earlier and more reliable warning of blocked catheters, makes the nurses' task less onerous, and provides a closed antiseptic system of drainage from the time of operation onwards. (We set the apparatus up in the theatre at the end of the operation.) We have not had any trouble from clot blocking the openings in the small jar, and it is never necessary to remove the lid from the apparatus during use, save to change the large container when full.

The apparatus is now being made for us by Messrs. Charles Thackray, 38, Welbeck Street, London, and is to be known as the King's College Hospital (K.C.H.) Drainage Bottle. All the metal parts are of chromium-plated brass. The cradle (fig. 2) is also being made by this firm.

Our thanks are due to Mr. J. G. Yates-Bell, F.R.C.S., for the initial stimulus to design this apparatus and for his continued help and encouragement; to Messrs. Thackray; and most importantly to the Ward Sister and her nurses for their coöperation.

N. A. STEPHENS
M.B. Lond., F.R.C.S.
C. Q. HENRIQUES
M.CHIR. Camb., F.R.C.S.
King's College Hospital, London

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Reviews of Books

A Short History of Public Health

C. FRASER BROCKINGTON, M.D., M.SC., barrister-at-Law, professor of social and preventive medicine, University of Manchester. London: J. & A. Churchill. 1956. Pp. 235. 15*s*.

IT was a good idea to write a short history of public health and bring it up to date. Developments can now be seen in the oblique light of the National Health Service Act. The first third of the book deals with the march of public-health history, and Professor Brockington shows a keen critical sense in his approach. The second part goes into greater detail over special aspects of the story, with emphasis on subjects of current interest. There is a critical account of economic and social changes in the past century, and their effect on mortality and population. The difficulty of housing is clearly seen in its historical perspective, and a proper assessment is made of the present-day situation. It is valuable to have such a sharply outlined sketch of slums and overcrowding. Professor Brockington also gives a useful account of the services for disorders of the mind; and he pays particular attention to the problems of today affecting the care of the aged.

This is a good book for the student of preventive medicine—an entire textbook for the undergraduate and a critical summary for the diploma student. The student of social science will also find it very helpful.

Ten Patients and an Almoner

FLORA BECK. London: Allen & Unwin. 1956. Pp. 159. 12*s*. 6*d*.

THIS book, which has a foreword by Prof. L. J. Witts, illustrates by ten imagined cases the functions and difficulties of a hospital almoner. Miss Allen is the young and relatively inexperienced almoner to the medical unit of the Chesilfield Infirmary, headed by Professor Harris, a tolerant and clear-headed clinical research-worker, and his first assistant, Dr. Graham, whose mistrust and resentment of the almoner runs through the book. There is also the wise and shrewd head almoner, Miss Chadd, who does a great deal to bring Miss Allen face to face with her limitations. The case-histories are described from the almoner's angle; her successes and mistakes are honestly set out; and at the end there is a long discussion between the four protagonists to try to arrive at a common policy for the use of the almoner by the medical unit. Unfortunately the whole book is set in the middle and later period of the war, before the advent of the National Health Service and the related social welfare legislation. It thus loses greatly in contemporary relevance, and many of the problems, such as compassionate leave for soldiers, eligibility for Public Assistance, and the inadequacy of National Health Insurance, have already a period flavour. Many of the histories, too, seem scrappy, and Miss Allen's ideas of social case-work often make one sympathise with the hostile Dr. Graham more than the author intended. Even the long discussion at the end does not get us very far, and the wisdom of Miss Chadd and the clear-headedness of Professor Harris are not as convincing as they might be. But the subject is an important one which concerns many doctors, and this is an arresting way of presenting it.

The Biliary Tract

With Special Reference to the Common Bile Duct. JULIAN A. STERLING, M.D., SC.D., F.A.C.S., staff surgeon, Albert Einstein Medical Center, Philadelphia. Baltimore: Williams & Wilkins. London: Baillière, Tindall, & Cox. 1955. Pp. 423. 80*s*.

THIS is an interesting but uneven book. It starts superbly with what is often the dreariest chapter of clinical monographs—the anatomy of the part. The anatomy of the biliary tree is still taboo in some of the best anatomical circles. Here Nature, so wonderfully constant in moulding other parts of the human body, seems to have gone astray; and her inconsistencies are to be deplored rather than explored. The author challenges this attitude with tremendous verve. Writing in a direct, clear style—the hallmark of familiarity—he gives the most accurate and readable account of the anatomy of the biliary tree hitherto published. Woolliness of thought and language (such as the current habit of describing the ampulla of Vater as a mass rather than a space) arouses his wrath—and rightly so. Surgical treatment here must be based on a clear understanding of the anatomy; and new operations cannot be assessed without appreciating the various structures which enter into the formation of this complex junctional area.

Unfortunately, after this splendid start, the book falls away to the level of one of those above-pass-mark higher-examination papers that often serve for "collective reviews." Long lists, catalogues, and unselected bibliography struggle to fill a clinical vacuum. The mysterious subject of pancreatitis opens promisingly enough with the dismissal of dozens of suggested ætiologies as "absurd," and of no less than 66 different forms of treatment as "too many." But the author has little better to offer. Many will question the unqualified advocacy of total pancreatectomy, duodenectomy, and partial gastrectomy for tumours of the body of the pancreas; and the important problem of palliation in biliary-tract surgery should perhaps have received more notice.

The chapter on radiology gains by its brevity: it is an up-to-date, clear, and practical account of many of the techniques which have been elaborated in America. To clinicians, dissatisfied with present diagnostic methods, this part of the book will be welcome. Finally, the chapter on the postcholecystectomy syndrome gives a faithful picture of the prevailing uncertainty.

Neurological Nursing

A Practical Guide. JOHN MARSHALL, M.D., M.R.C.P., senior lecturer in neurology, University of Edinburgh. Oxford: Blackwell Scientific Publications. 1956. Pp. 166. 18*s*. 6*d*.

THE nursing of patients in a neurological unit requires special aptitudes and skills. Although it may be very rewarding to care for patients with acute neurological illness, the nurse is apt to be disheartened by the steady decline, despite her efforts, of those with chronic incurable diseases of the nervous system. As Dr. Marshall rightly points out, it is in the chronic cases that the help of the nurse may most be needed. His book succeeds admirably in its dual aim of presenting the nurse's duties in a practical way and of arousing interest in the subject.

Written in simple clear terms, its format is attractive, and the illustrations are well chosen and for the most part well reproduced (although the radiographs, and particularly the air encephalograms, could be better). The chapter on respiratory difficulties is particularly good.

There are, however, some important omissions. Although the drug treatment of epilepsy is considered in detail, the relief of pain or headache and the control of restlessness or abnormal behaviour are barely mentioned. There is no guidance on the nursing care of patients with prolapsed intervertebral discs. The management of barbiturate poisoning and alcoholism might also have had more attention; and in the chapter on special investigations electromyography and injection techniques (of the trigeminal or stellate ganglia) should perhaps be mentioned if the author's aim is not only to train the nurse as an assistant but to interest her in ancillary methods of neurological diagnosis. It would also be useful to include more definitions or a glossary of neurological terms. In the section on examination, it would be of interest to include descriptions of some of the characteristic abnormal gaits.

Dr. Marshall's book will be rightly popular and should be studied by every nurse who has to take care of neurological cases.

The Principles and Practice of Medicine (3rd ed. Edinburgh: E. & S. Livingstone. 1956. Pp. 1076. 35*s*.).—The demand for a third edition (the first appeared as recently as 1952) is a triumph for Sir Stanley Davidson and the staff of the Edinburgh department of medicine and the others who have helped to produce this book. The section on neurology has been rewritten; and the inevitable additions necessary to keep up with events have added slightly to the book's size. The price has also edged up a few points.

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THE LANCET

LONDON: SATURDAY, SEPT. 15, 1956

The Tainted Thermometer

IT is remarkable that every patient in hospital has his temperature taken at least twice a day. Other instruments of diagnosis are used only if they provide information relevant to the patient's illness; but this discrimination is seldom applied to the taking of temperatures. It is a pity, therefore, that in many hospitals the hygiene of temperature-taking is less efficient than it might be. A busy nurse in a ward of 30 patients may use no more than half a dozen thermometers, each of them spending only a few moments in a pink fluid before passing from one patient to another. The Medical Research Council committee on cross-infection in hospitals [1] recommended that each patient should have a separate thermometer. Few nurses or doctors and still fewer patients will disagree with this advice, yet GOODALL,[2] in 1952, found that of 19 wards he visited only 3 provided individual thermometers. Bacteriological objections to the communal thermometer are that it may convey such infections as tuberculosis, diphtheria, scarlet fever, poliomyelitis, "sore throat," influenza, and the common cold. It may help to disseminate the hospital strains of antibiotic-resistant staphylococci that now inhabit the respiratory tracts of so many patients. Bacteriology apart, there is a strong æsthetic objection to poking into one's mouth an instrument which, a few moments ago, was sticking out of someone else's.

Objections to the communal thermometer would be less forcible if it was effectively cleaned and sterilised after use; but the speed at which a thermometer round is conducted makes this almost impossible to achieve. Many of the fluids in which thermometers are traditionally immersed have only feeble disinfecting powers. Glycerinum thymolis co. is one of the most popular thermometer disinfectants, but GREEN and PENFOLD [3] have shown that bacteria can survive in it for twenty-four hours. Phenolic fluids are possibly more effective, but they are less popular because inaccurately dispensed solutions, if not properly washed from the thermometer, may be dangerous. They also have the inconvenient property of removing the ink markings from the engraved graduations. 1 in 1000 biniodide of mercury is widely used, and MIRVISH [4] has lately examined communal thermometers kept in this solution. After four hours' immersion—a much longer period than is possible during a ward temperature round—bacteria were grown from 28 out of 51 oral thermometers and from 35 out of 58 rectal thermometers. Most of the organisms were non-pathogens, but *Staphylococcus aureus* and hæmolytic streptococci were also isolated. It seems possible that other pathogens would have been found if the wards had happened to contain patients harbouring them and if suitable culture methods had been used. MIRVISH does not give full details of his bacteriological methods, but it seems he did not use those suitable for the growth of tubercle bacilli and viruses. But the precise organisms isolated are relatively unimportant compared with the finding that sterilisation was inadequate.

It can be argued that the need is for individual thermometers or rapid efficient disinfection, and that to provide both is not necessary. This may be true, but there is much to be said for taking the double precaution. The selection of a fluid for disinfecting thermometers is usually made by a clinician or a ward sister, and it is time that they were given reliable bacteriological guidance in making this choice. Unfortunately many disinfection experiments in the past have been invalid because precautions were not taken to neutralise the disinfectant before making the cultures. This precaution was not overlooked by FROBISHER et al.,[5] who made cultures for tubercle bacilli and other organisms (though not viruses) from thermometers that had been artificially contaminated with infected sputum. They found that 1 in 1000 alcoholic solutions of quaternary ammonium compounds and 0·5% tincture of iodine gave complete sterilisation after ten minutes' immersion, and that the performances of all disinfectants in the trial were improved if the thermometers were wiped with a piece of soapy cotton-wool before being put into the fluid. Although alcohol itself was unreliable, disinfectants dissolved in 70% spirit were more effective than aqueous solutions, and for this purpose the cheaper isopropyl alcohol was just as effective as ethyl alcohol. At the other extreme, formalin gave particularly bad results. Iodine is expensive and some people are sensitive to it; but MIRVISH finds that two quaternary ammonium compounds, cetrimide and benzalkonium chloride, are non-irritant. Their ability to do all that is needed in this field is still unproven, but they deserve a proper trial. Meanwhile, there is no justification for further delay in providing each hospital patient with a separate clinical thermometer.

Cigarette Tar

IF cigarette smoking is a cause of lung cancer, as the statistical evidence indicates,[6] what is the substance in cigarette smoke which makes it dangerous? To answer this question the products of smoking—tar and particles—must be collected by the artificial smoking of cigarettes under conditions which simulate the human habit so far as possible. For this reason continued efforts are being made to determine these conditions more precisely. Since we last referred [7] to this work, some further progress has been made. ERMALA and HOLSTI,[8] using a silver-constantan thermocouple, found that the temperature in the combustion zone of a cigarette averaged 650°C (the range was 470–812°C), whereas in the relatively harmless pipe it was 500°C (range 380–620°C). With an iron-constantan thermocouple LYONS [9] found that the range in normal quiet cigarette puffing was 580–650°C; drawing on the cigarette at intervals of

1. The Control of Cross-infection in Hospital. Medical Research Council. War memorandum no. 11. H.M. Stationery Office 1944. Revised edition, 1951.
2. Goodall, J. W. D. *Lancet*, 1952, i, 807.
3. Green, J. B. M., Penfold, J. B. *Ibid*, 1947, ii, 89.
4. Mirvish, I. *S. Afr. med. J.* 1956, **30**, 413.
5. Frobisher, M., Sommermeyer, L., Blackwell, M. J. *Appl. Microbiol.* 1953, **1**, 187.
6. See *Lancet*, 1956, i, 678.
7. *Ibid*, 1956, p. 1004.
8. Ermala, P., Holsti, L. R. *Cancer Res.* 1956, **16**, 490.
9. Lyons, M. J. British Empire Cancer Campaign. 23rd annual report, 1955.

2–4 seconds raised the temperature to an average of 750°C. Thus, there is now substantial agreement on the temperatures reached during habitual smoking. At such temperatures carcinogenic hydrocarbons are formed from organic matter, and in fact several workers have detected benzpyrene in the tar. Some of this compound may be destroyed under the same conditions.[9] Other suspected substances include phenols, which have been found to be carcinogenic to mouse skin,[10] certain chemicals existing as free radicals according to GREENE,[11] and arsenic, which has increased by 300% in American-tobacco cigarettes[12] between 1932 and 1951 as a result of the use of arsenic in the control of pests. Another possibility is that cigarette tar acts as a promoter rather than an initiator in carcinogenesis.[13] Unfortunately, in a test designed to detect this action, so much initiator was used, in the form of benzpyrene, that no satisfactory answer was obtained.

When the tar has been collected under proper conditions, the next step is to try to isolate known carcinogens or to test the crude tar for its carcinogenic properties in animals. Both courses have led to an impasse. Benzpyrene has been detected and measured by several observers. Tumours have been induced in mouse skin by some but not most of those who have tried; and one group have produced tumours in rabbit skin. Are any of these findings relevant to the problem of human lung cancer? It is not now adequate to describe an agent as a carcinogen without saying to what, to whom, and in what amount. Benzpyrene is not carcinogenic to all tissues of all animals. The only test reported in man was negative, but possibly its duration was inadequate.[14] The characteristic hyperplasia induced by benzpyrene in human fœtal lung surviving in culture is suggestive but not conclusive evidence of carcinogenic potency in man.[15] Positive responses in animal tissues are the best guide we have, but they do no more than serve as a warning.

Apart from any possible relationship with lung cancer, there is evidence of other harmful actions of cigarette tar. Immediate and late effects at the site of deposition of tobacco smoke and tar are being investigated.[16] An immediate visible effect is the cessation of ciliary action when the toxic substances are in sufficiently high concentration. These substances are then dissolved and absorbed into the mucous membrane,[17] and they include carcinogens for animals.[16] The late effects include increased thickness and metaplasia of bronchial epithelium.[18]

We are a long way from deciding just what smoking does to the bronchial mucosa. But that is no reason for being hesitant in putting the known facts before the public and in dissuading young people from starting to smoke. One way of deterring them might be to let them see and smell this malodorous and nauseous tar, which, if appearance is anything to go by, is likely to prove the evil-doer.

10. Bontwell, R. K., Rusch, H. P., Booth, B. *Proc. Amer. Ass. Cancer Res.* 1956, **2**, 96.
11. Greene, C. R. *Science*, 1956, **123**, 227.
12. Satterlee, H. S. *New Engl. J. Med.* 1956, **254**, 1149.
13. Gellhorn, A., Klausner, C., Hibbert, J. *Proc. Amer. Ass. Cancer Res.* 1956, **2**, 109.
14. Cottini, G. B., Mazzone, G. B. *Amer. J. Cancer*, 1939, **37**, 186.
15. Lasnitzki, I. *J. Path. Bact.* 1956, **71**, 262.
16. Kotin, P., Falk, H. *Proc. Amer. Ass. Cancer Res.* 1956, **2**, 127.
17. Hilding, A. C. *New Engl. J. Med.* 1956, **254**, 1155.
18. Chang, S. C. *Proc. Amer. Ass. Cancer Res.* 1956, **2**, 99.

The Almoner

MEDICAL students are (or should be) continually exhorted to "treat the patient and not the disease." This is especially necessary because their main experience is of acute general hospitals where each patient comes under observation for a relatively short time and is isolated from his background—his home, family, and work. In these circumstances it is fatally easy to get into the habit of referring to "the case of tuberculosis in bed 4," or "the Charcot-Marie-Tooth disease in the corner," and to forget that the young mother's long illness and potential infectiveness may have shattering effects on her family, while the boy's stiff back means that his career must be completely replanned. The family doctor, meeting and treating his patients over many years, is in much less danger; but he may find himself unable to give such problems the thought and time they need. No good doctor who cares about his patients would question that these things are a part of his total clinical responsibility; but to unravel the knots created by an illness may require a number of interviews with the patient himself, his relatives, and even his employers or school teachers. Not only does this take much time but the doctor himself would seldom claim detailed knowledge of the social agencies and potentialities needed for handling the more complex cases. Can he, and should he, delegate this part of his job to specially trained workers, as he has already delegated other parts to nurses, physiotherapists, pharmacists, and the like?

Those with experience of good medicosocial work would agree that he can and should. The hospital almoner, the psychiatric social worker, and (in a slightly different context) the health visitor are all trained for such work and, in varying degree, ready to his hand. The psychiatrist has long accepted such help, and his main complaint is that there are not enough psychiatric social workers; he relies on them to supplement his own history-taking, to tell him about home and working conditions, and to help in the patient's re-establishment and support after treatment. In many hospitals the almoner occupies a similar position, but only too often she still meets with hostility from medical staff who fear that she may trespass on their territory. It seems strange that there should still be such misunderstanding when the profession has been in existence for more than fifty years and has been so completely accepted by so many doctors. Sometimes inexperienced or inadequate almoners have themselves contributed, by excessive assertion of their independence or by jealousy in guarding their information; but most often medical hostility is explained by failure to recognise what the almoner's function is—chiefly because the opponents have never had the experience of working with a good almoner. How common such lack of experience must be is shown by the fact that in 1952 almoners were employed at only 349 of the 917 general (or mainly general) hospitals in England and Wales.

The book by Miss FLORA BECK which we review this week is an interesting if not fully successful attempt to further the mutual understanding of doctors and almoners; and certainly this understanding must be improved if the patient's needs are to be met without waste of medical time. The almoner's techniques, her habit of helping the patient to solve his

own problems rather than telling him how to solve them, and her wide knowledge of social resources are all valuable to the hospital doctor, anxious to treat the whole patient. And what of the general practitioner? One of the defects of Miss BECK's book, as we see it, is that it does not emphasise the need to consult the patient's own doctor: indeed the almoner in her stories visits patients' homes, far from her base, apparently without any communication with the practitioner either from the hospital medical staff or herself—which clearly would not be good practice. Help comparable to what is given to the hospital doctor by the almoner should be given to the family doctor by the health visitor—the third member of the medicosocial team. If the recommendations of the Working Party[1] are fulfilled, the health visitor's relations with the family and with the family doctor should be such that she can give the almoner information and help, and also get information and help from the almoner about patients coming out of hospital. This is additional to her other function, with the medical officer of health and her other colleagues in the health department, of ensuring that necessary personal and environmental assistance is provided.

In general practice as in the hospital, there is often need for several kinds of help, and they should not be given in isolation. The whole patient is apt to need the whole team.

Annotations

DEAF OR BACKWARD?

IT has been said that if a child is not speaking by the age of two it is likely to be either deaf or backward; and the distinction between deafness and mental defect, in all their degrees, is not always easy. There can be no doubt that some children who are partially deaf have, in the past, been assessed (quite wrongly) as backward children and admitted to schools for the educationally subnormal. The fault lies in the methods of testing and applies mainly to children with deafness for high tones. Since many of these children have good or even normal hearing for low tones, deafness is often unsuspected as the cause of their failure to advance; and verbal tests of intelligence may therefore be applied. Such verbal tests are always likely to give a low estimate of intelligence in the child with a high-tone deafness. Peformance tests, on the other hand, will give a more accurate idea of intelligence, and any wide discrepancy between the results of performance tests and verbal tests should always arouse suspicion of an underlying defect of hearing. Another diagnosis sometimes made in the partially deaf child who is not speaking properly is that of congenital auditory imperception—a form of aphasia or "word-deafness." But many children who have been so labelled have later been shown to suffer from partial deafness, again usually for high tones.

Even more serious is the group of deaf children who spend their lives in institutions for mental defectives. Neurotic reactions may be common among deaf children, as the result of their deafness and consequent frustration; these include enuresis, fæcal incontinence, screaming attacks, and tantrums. In March, 1953, a research unit was established at Belmont Hospital, Sutton, Surrey, for the study of apparently deaf children with defective speech and behaviour problems. The primary aim of the unit was to try to assess whether children who had acquired no speech were deaf, mentally defective, emotionally disturbed, or suffering from a combination of these or other conditions. Dawson et al.[1] have lately given a preliminary report of their observations on 22 such children. They point out "that some children who have never spoken and who are therefore inaccessible and who may be asocial or antisocial in their behaviour are diagnosed as being mentally defective and spend their lives in mentally defective institutions." But it has already been shown in the Belmont unit that a number of these children prove, after a period of observation, to be deaf and probably educable. "If facilities were available to continue their education under specialised conditions they could no doubt make useful citizens within their limitations." 19 of the 22 children did not speak at all and superficially all of them seemed to be deaf. Congenital abnormalities were present in 11. When they were admitted, most of the children were emotionally disturbed and gave no indication of their true potentialities. This difficulty had to be at least partly overcome before the child's disability could be assessed. The child's reactions to its environment and to its teaching played a large part in determining whether its backwardness was due to deafness or mental defect. When the confidence and coöperation of the child had been gained, tests of hearing and of educational ability were started.

The ability to assess hearing must, of course, depend upon some positive and objective response to an auditory stimulus and some idea of the child's hearing could usually be formed by day-to-day observation. The simple conditioned play responses devised by the Ewings were used, but other electrophysiological methods were also applied. These included pure-tone audiometry, electro-encephalography, and psychogalvanometry, but none gave a wholly reliable estimate of the child's hearing. (It is interesting that 9 of the 11 children with congenital abnormalities were finally considered to be either totally or partially deaf.) Mental ability was assessed by the Merrill-Palmer preschool scale and the Drever-Collins battery, both of which can be used without the need for the examiner or the examinee to speak.

Even more important, however, was the assessment of the educational ability of these children; for these were children who had been regarded as ineducable. 14 of the 22 children showed improvement in coöperation and awareness over periods ranging from three to twelve months, and 4 of these were judged to be sufficiently stable to take their place in normal schools for the deaf. Dawson et al. hope that even more of these children might ultimately be trained to do some sort of work at which they could earn a living. The earlier these children can be assessed and taught, the better are their chances of responding to teaching. As Dawson et al. put it, "these children present a most difficult problem but certainly not one which can be dismissed. There is yet no means of making a satisfactory diagnosis, but it is already felt that much can be done over a period of time to assess their condition and educability and that where there is any doubt about a child it is entitled to a period of observation."

NON-EXPLOSIVE ANÆSTHETICS

THE need for an all-purpose but non-explosive inhalation anæsthetic is clear,[2] and the search goes on.[3] The most recent development lies in the clinical investigation of the fluorinated ethers. Fluorination diminishes the inflammability, and also unfortunately the potency, of these anæsthetics; but by treating ethyl vinyl ether in

1. An Inquiry into Health Visiting. Report of a Working Party on the Field of Work, Training and Recruitment of Health Visitors. H.M. Stationery Office. 1956. Pp. 183. 6s. 6d. See *Lancet*, 1956, i, 908.

1. Dawson, M. E., Evans, M. J., Reed, M., Minski, L. *J. ment. Sci.* 1956, **102**, 121.
2. See *Lancet*, Aug. 18, 1956, p. 352.
3. *Ibid*, 1956, i, 321.

this way a compound has been produced which can be used as an anæsthetic.

Sadove et al.[4] have lately described a clinical trial of trifluoroethylvinyl ether, known in the United States as 'Fluoromar.' The drug seems safe: the heart and blood-pressure were not significantly affected, and postoperative sickness was slight. Liver-function tests on a number of patients showed no definite changes. The blood and respiratory gas levels of the anæsthetic were measured at various stages of narcosis and they showed that it was potent, though once consciousness is lost surgical anæsthesia takes some time to achieve. In these respects fluoromar apparently resembles ethyl ether, though its physical properties differ. It is, however, in the matter of inflammability that fluoromar falls short of expectation, since it is still inflammable within the range of concentrations likely to be used for anæsthesia, though less so than ethyl ether or cyclopropane. Nevertheless, it marks a further step toward the ultimate ideal.

MEASURES OF PREVENTION

THE dividends of preventive medicine are less obvious than those of active medical or surgical treatment: there is no falling temperature, no healing wound, and few thanks. It may be therefore that the family doctor is discouraged from doing much about the preventive side of his work by the lack of prompt returns. But he can take heart from the fact that the statistical method, applied to public-health measures, is beginning to come into its own by demonstrating on the broader scale the results of preventive action. Much of the improvement in the nation's health is due to the work of the family doctor, though the contribution of the individual is lost in the bulk figures for diminished morbidity in many fields; and there are few ways in which the general practitioner can measure his own efficiency as a health teacher, or, for that matter, few means whereby the total contribution of the work of general practitioners can be assessed.

What are the hints that may lead a family doctor to believe that his teaching is getting home? An increase in the number of those who consult him with a question rather than a symptom; more consultations by young mothers and their children; fewer calls for visits (and many fewer unnecessary ones); less demand for medication; and, above all, a definite decrease in the number of items of service which the doctor performs without a proportional falling-off in the size of his medical list. The ratio of items of service to total of patients is one of the few measurable values, and the doctor can calculate for himself the effects of his own teaching in terms of time saved—time which will enable him to raise his standards of diagnosis and treatment. Analysis of items of service by content may show less trivialities, and more patients may seek the doctor's advice rather than his medicine, though collected figures on this point may be misleading.

Certain prophylactic measures, such as immunisation (for which the family doctor will have increasing scope), provide another measurable value. The number of children in a practice who reach school age fully immunised by contemporary standards is one measure of the preventive thinking in that practice. Vaccination against smallpox is also a broader guide; and the very low vaccination-rates in some parts of the country are a reproach to the doctors in practice there. Where advice about vaccination has not come from the family doctor, it is unlikely that the mother will ask for it herself.

Some of the measurable changes which reflect the success or failure of preventive efforts are under continuous review by the medical officer of health; but there are others which can be watched only by the general practitioner. Both would benefit from study of this problem together, and many medical officers of health could usefully collaborate with family doctors in statistical analyses of morbidity and other figures. The statistical resources of the public-health department could not be better used than in the measurement of what can be achieved by preventive general practice.

4. Sadove, M. S., Balagot, R. C., Linde, H. W. *Anesthesiology*, 1956, **17**, 591.

REPLACEMENT OF RENAL ARTERIES

IT is now well established that the diseased aorta can be replaced, with an expectation of reasonable success, by homo and auto arterial grafts and by many types of tubes manufactured from man-made fibres. Recently Horton et al.[1] have recorded their experiences with autogenous skin used to repair arterial defects. In 12 dogs, jackets of skin used to reinforce the wall of the aorta grew and functioned without difficulty giving, the authors claim, additional strength to the vessel wall and presumably reducing the risk of aneurysm. When the skin formed the tubular graft itself the results were less convincing.

Interest and activity in arterial replacement continues unabated. Many clinicians must have wondered whether the upper limits of aortic excision could not be extended to include the renal arteries, which are themselves often involved in aneurysmal dilatation or narrowed by atheromatous deposits; and indeed reports from many centres are concerned with these problems. Schilling et al.[2] describe their technique, worked out in dogs, for aortic homografting, including the renal arteries. These operations were performed without hypotension or cooling under pentobarbitone anæsthesia, and the homografts were stored before use in Tyrode's solution. The technical difficulties of aortic-renal replacement in the dog are formidable, because the renal arteries are small and the right one is relatively inaccessible. 5 out of 8 dogs died shortly after operation, 4 from bilateral thrombosis of the renal vessels and 1 from an overdose of heparin. In the 3 that survived the blood-urea level was high when they were sacrificed over six months later, and all the kidneys examined showed fibrosis and glomerular obliteration. This is not surprising considering that the anastomosis took well over an hour and the total period of renal ischæmia was up to eighty minutes.

Poutasse et al.[3] describe their findings in 3 patients suffering from severe hypertension due to bilateral stenosis of the renal arteries. All 3 were young (14, 15, and 25 years) and the renal arteries of each were obstructed by fibrous intimal proliferation. The eldest also had extensive aortic atherosclerosis with an aneurysm of the abdominal aorta. 2 patients rapidly succumbed to their disease. The third, a boy of 15, is of considerable surgical interest. He had moderately severe hypertension with mild constriction of the retinal arterioles. An intravenous pyelogram showed no significant structural or functional abnormality of the kidneys. Aortography, nevertheless, disclosed gross narrowing of the origin of both renal arteries with some dilatation beyond the strictures.

A freeze-dried femoral-artery homograft was sutured to the aorta end-to-side just below the renal artery, whose narrow segment was ligated and excised. The homograft was then sutured end-to-end to the normal portion of the renal artery close to the hilus. The kidney circulation was interrupted for only five minutes. With the reconstituted blood-flow the kidney returned to normal colour and recovery was uneventful. The other

1. Horton, C., Campbell, F., Connar, R., Smith, A., Pickrell, K. *Surgery*, 1956, **39**, 926.
2. Schilling, J. A., Becker, E. L., Bowers, C. R., Gold, D. *Ibid.* p. 611.
3. Poutasse, E. F., Humphries, A. W., McCormack, L. J., Corcoran, A. C. *J. Amer. med. Ass.* 1956, **161**, 419.

narrowed renal artery was similarly dealt with at a second successful operation. Postoperative aortography showed both renal arteries to be functioning normally without constriction or impairment of renal flow. The blood-pressure gradually fell and the diastolic six weeks later was about 30 mm. Hg below the preoperative level; renal function tests were unimpaired. The boy has remained well.

Poutasse et al. suggest that the hypertension in all 3 patients was caused by stenosis of the renal arteries due to a developmental flaw. Their report suggests two things: narrowing of the renal arteries must be considered as a cause of juvenile hypertension, which can be detected only by aortography; and the indications for arterial grafting are now even wider and call for the closest coöperation between physician and surgeon.

CHLORPROMAZINE IN OBSTETRICS

THE diversity of the pharmacological actions of chlorpromazine has suggested to many people that this antihistamine may be of value in obstetrics. First, it may have a central "tranquillising" action; secondly, it may potentiate and prolong the action of analgesic drugs so that smaller doses are effective; and, thirdly, it may prevent vomiting of pregnancy.

The sedative action of chlorpromazine during labour is good, though once a total dosage of 75 mg. is approached the mother is likely to become indifferent to her surroundings and less coöperative than is normally desirable. Effective analgesia can be produced by a mixture of 25 mg. of chlorpromazine and 50 mg. of pethidine (about half the usual dose of pethidine), and this combination can be repeated when necessary. It should be given by deep intramuscular injection. A small dose of scopolamine (gr. $^1/_{200}$) will then produce amnesia if that is what is wanted, since this action is also potentiated by chlorpromazine.

There is no doubt that the mixture is effective in producing analgesia, but when compared with the more usual means of doing so in labour, such as pethidine alone, pethidine and a barbiturate, or similar combinations with scopolamine, there is little or no difference in the result so far as the mother is concerned.[1 2] Any advantage must be sought in the effect on the baby. Here results are conflicting, though all workers agree that chlorpromazine does no harm to the child. A significant decrease in the incidence of neonatal asphyxia has been attributed to the reduced dosage of analgesics [3 4]; but others disagree.[2] Nausea and vomiting, however, both in early pregnancy and during labour, can be effectively treated with chlorpromazine.

Among the possible disadvantages, the action of chlorpromazine on uterine contraction is of considerable importance. Provided the dose is kept below 75 mg., labour is not prolonged, though in the second stage the active expulsive efforts of the mother may be poor, and the number of forceps deliveries may increase in consequence.[1] The third stage of labour is not affected. The hypotension caused by chlorpromazine is slight in the recumbent position and does not matter provided the patient is warned not to sit up. It may, however, be a bar to the use of the drug for patients with essential hypertension or hypertension due to toxæmia of pregnancy. The total dose given in labour is so small that the danger of jaundice from liver damage can be disregarded; but the same cannot be said when treating hyperemesis for long periods.

Though it seems promising, chlorpromazine must be further investigated before its use in obstetrics can be accepted without reserve. It seems likely to be of particular value for certain types of patient, especially when there are reasons for avoiding narcotic or analgesic drugs or for giving them only in very small doses.

1. Savage, D. *Brit. J. Anæsth.* 1955, **27**, 346.
2. Norton, H. I., Weingarten, M., McDonough, E. T. *Amer. J. Obstet. Gynec.* 1956, **71**, 1251.
3. Anz, U. E., Smith, L. J. *Ibid*, p. 1242.
4. Schaffer, A. L. *Ibid*, p. 1247.

NOVOBIOCIN

SINCE the announcement of the discovery of novobiocin at the third annual antibiotic symposium in Washington last November,[1] bacteriological and clinical investigations have confirmed that it is a relatively non-toxic antibiotic which promises to be of particular value in staphylococcal infections. It has also been called streptonivicin, 'Cathomycin,' 'Albamycin,' and 'Cardelmycin.' It has no connection with the apparently dissimilar Russian antibiotic, albomycin.[2 3] The confusion in terminology arose because streptonivicin and cathomycin were independently isolated from cultures of two actinomycetes, *Streptomyces niveus* and *Strep. spheroides*. Their ultra-violet and infra-red absorption spectra, and some of their other physical properties, have since established that they are the same [4]; and the generic name, novobiocin, has now been adopted.

Novobiocin can be given by mouth in doses of 500 mg. (2 capsules) every six hours, intravenously in a similar dose every twelve hours, or intramuscularly 250 mg. every eight hours. It is rapidly absorbed and peak serum concentrations are reached in two hours if it has been taken on an empty stomach. The antibiotic is largely bound to protein in the blood, principally to serum-albumin; but this is presumably a loose linkage since high urinary concentrations appear within eight hours of absorption. In-vitro studies show that, in the presence of 10% of human serum, 50–95% of antibacterial activity is lost: but since the antibiotic can be recovered unimpaired by extraction of the serum, it does not seem to be altered or destroyed by this contact.[5] It diffuses into pleural and peritoneal cavities but it does not apparently cross the blood-brain barrier. Part of a dose is excreted in the bile.

The bacteriostatic range is chiefly against gram-positive cocci; it is ineffective against gram-negative organisms, with the possible exception of species of proteus, which may be moderately sensitive in vitro. Although novobiocin has cured anthrax [6] and has subdued pneumococcal and streptococcal infections, its chief value is in the control of staphylococci. Since it shows no cross-resistance with penicillin, streptomycin, chloramphenicol, the tetracycline drugs, neomycin, bacitracin, or erythromycin,[7] its chief indication will probably be for staphylococcal infections which cannot be controlled by other antibiotics. Clinical trials are being conducted to see whether its use in combination with other antibiotics, notably erythromycin, may hamper the emergence of resistant staphylococci.[8]

Novobiocin has had mild toxic effects, of which the commonest and most troublesome are rashes and drug fever. There may be gastro-intestinal upsets, but it is unlikely that it will cause staphylococcal enterocolitis because the fæcal flora is unchanged in its content of gram-negative bacilli, yeasts, and clostridia. Indeed, novobiocin has been effective in the treatment of staphylococcal enterocolitis.[7] There has been no evidence of

1. Antibiotics Annual, 1955–1956. New York, 1956; pp. 909, 918, 924.
2. Gause, G. F. *Brit. med. J.* 1955, ii, 1177.
3. Correspondence correcting our own mistake over the relation of novobiocin to albomycin appeared in our issues of March 17 (p. 330) and April 14 (p. 450).
4. Welch, H., Wright, W. W. *Antibiot. Chemother.* 1955, **5**, 670.
5. Simon, H. J., McCune, R. M., Dineen, P. A. P., Rogers, D. E. *Antibiot. Med.* 1956, **11**, 205.
6. Lin, F. K., Coriell, L. L. *Ibid*, p. 268.
7. Martin, W. J., Heilman, F. R., Nichol, D. R., Wellman, W. E., Geraci, J. E. *Ibid*, p. 258.
8. Nichols, R. L., Finland, M. *Ibid*, p. 241.

damage to the blood, kidneys, or liver. A raised icteric index has been noted during treatment, but this may be due to a yellow pigment metabolite of novobiocin.

TRANSAMINASE IN ISCHÆMIC HEART-DISEASE

WHILE studying transamination in intermediary metabolism, Cohen and Hekhuis [1] noted that transaminase activity was greater in heart-muscle than in other tissues. Some years later LaDue et al.[2] investigated the activity of serum glutamic-oxalacetic transaminase in various human diseases, using a spectrophotometric method.[3] They found that the serum-transaminase activity was much above normal about twenty-four hours after cardiac infarction; it returned to normal within a few days. Important questions were whether other conditions, especially those which might clinically be confused with cardiac infarction, were accompanied by comparable elevation of the serum-transaminase level, and whether the raised level reflected the amount of myocardium destroyed.

Agress et al.[4 5] observed the effect of experimental myocardial infarction on serum-transaminase. The concentration rose rapidly in dogs; and the changes suggested a linear relationship between the peak level and the amount of infarcted myocardium at necropsy. This work was confirmed,[6] and the infarcted muscle was found to contain less transaminase than adjacent healthy muscle.

Many workers have reported increased serum-transaminase in the presence of liver disease [7–11] and in pancreatitis.[7 8 12] If the level of serum-transaminase is to be used clinically to supplement the electrocardiogram in the qualitative diagnosis of cardiac infarction, this matters less than the finding of a raised serum-transaminase after pulmonary embolism,[8] although this has not been found in experimental pulmonary infarction.[13] Further investigation of this important point is needed. Myocardial infarction may take place and yet no diagnostic change in serum-transaminase is found [8 9]; one such patient died before the peak level of transaminase was likely to have been reached, and it could be missed in others. Significant elevation has been found after very rapid cardiac arrhythmias [7] and after saddle embolus of the aorta.[10] Merrill and his colleagues [10] concluded that increases in serum-transaminase might be associated with cellular injury in various tissues.

The view [7] that estimation of serum-transaminase may be a useful guide in excluding, as opposed to diagnosing, myocardial necrosis is sound, if the test is done at the right time. Ultimately it may prove more helpful as a quantitative estimate of cardiac infarction than as a qualitative aid to existing methods of diagnosis. A recent report [12] showed that there was some overlap in the transaminase levels between patients with cardiac infarction and acute coronary insufficiency, and between those with acute coronary insufficiency and angina pectoris. Clinical details are lacking but presumably the angina pectoris was related to exertion. Some of those with angina pectoris had had past cardiac infarction and others had not. It may be that some of the patients considered to have acute coronary insufficiency, or angina pectoris, may have had undiagnosed subendocardial infarction. Alternatively, there is the possibility of myocardial necrosis with prolonged or severe angina pectoris.

At present the transaminase test seems to offer little as a supplement to the electrocardiogram in the diagnosis of cardiac infarction, particularly in differentiating subendocardial infarction from acute coronary insufficiency. Further studies on humans, with necropsy control, are necessary before the place of serum-transaminase, either as a qualitative diagnostic procedure or as a quantitative measure of cardiac infarction, can be accurately judged. Quantitatively it could prove valuable both in the clinical management of the patient and in prognosis.

1. Cohen, P. P., Hekhuis, G. L. *J. biol. Chem.* 1941, **140**, 711.
2. LaDue, J. S., Wróblewski, F., Karmen, A. *Science*, 1954, **120**, 497.
3. Karmen, A., Wróblewski, F., LaDue, J. S. *J. clin. Invest.* 1955, **34**, 126.
4. Agress, C. M., Jacobs, H. I., Glassner, H. F., Lederer, M. A., Clark, W. G., Wróblewski, F., Karmen, A., LaDue, J. S. *Circulation*, 1955, **11**, 711.
5. LaDue, J. S., Wróblewski, F. *Ibid*, p. 871.
6. Nydick, I., Wróblewski, F., LaDue, J. S. *Ibid*, 1955, **12**, 161.
7. Chinsky, M., Shmagranoff, G. L., Sherry, S. *J. Lab. clin. Med.* 1956, **47**, 108.
8. Denney, J. L., McAuley, C. B., Martin, H. E., Ware, A. G., Segalove, M. *J. Amer. med. Ass.* 1956, **161**, 614.
9. Kattus, A. A. jun., Watanabe, R., Semenson, C., Drell, W., Agress, C. *Ibid*, 1956, **160**, 16.
10. Merrill, J. M., Lemley-Stone, J., Grace, J. T. jun., Meneeley, G. R. *Ibid*, p. 1454.
11. Wróblewski, F., LaDue, J. S. *Ibid*, p. 1130.
12. Ruskin, A., Mahaffey, W. C., Ruskin, B. *Clin. res. Proc.* 1956, **4**, 30.
13. Agress, C. M., Glassner, H. F., Jacobs, H. I. *Circ. Res.* 1956, **4**, 220.

POLIOMYELITIS AND THE WEATHER

KNOWING what it does of the habits of whooping-cough and measles, the public at large finds it hard to understand the natural history of a disease, such as cerebrospinal fever, few of whose victims give any overt evidence of infection. To this characteristic poliomyelitis adds relative novelty, an apparent predilection for the young, and sometimes a fatal end. It is not surprising, therefore, that it is commonly thought of as a mysterious disease, whose incidence and effects are to be explained by processes outside the common experience of doctors as well as laymen. Suggestions in this direction have ranged from the helpful to the hopeless, but no-one would wish to suppress them. Outside our profession the miasmatic theory of disease is by no means dead, and the seasons are credited with powers for good and evil which are not entirely supported by vital statistics. Few epidemic diseases in fact show an incidence unchanged throughout the year—a remarkable fact in itself—and a good deal has been made of the observation that the maximum incidence of poliomyelitis coincides with that of the intestinal infections in the late summer. (Hypotheses based on this may have been premature, for there is no doubt that Sonne dysentery is now commonest in the spring.) It is in the late summer that counters and barrows are piled with Victorias and Worcesters; and, since fruit-pickers are sometimes none too strict about personal hygiene, it may be that raw fruit plays some part in the spread of infection.[1]

Attempts to associate epidemic poliomyelitis with meteorological phenomena such as temperature and humidity have been unproductive,[2] but recently Lawrence [3] has shown that the odds against the association of weekly and annual notifications with "accumulated degree weeks from a base of 60°F" being due to chance are between 20 and 50 to 1. It is a pity that he does not explain in simpler terms what this phrase means: we take it to mean that poliomyelitis is commoner in a hot summer. That is a very interesting observation, but its importance is doubtful. No-one yet knows whether notifications bear a constant ratio to infections, and until this point is settled the high proportion of symptomless infections detracts from the value of notifications as a measure of poliomyelitis. As far as is known, the virus is an obligatory parasite of homoiothermic animals and to judge from experience with bacteria the physical condition of the outside air concerns these very little. Before too much effort is expended on pursuing this line of inquiry, it might be of value to examine the correlation of the "accumulated degree weeks for a base 60°F" with the sales of soft drinks, the flowering of dahlias, and the averages of the leading fast bowlers.

1. Silverton, M. I. *Med. Offr*, 1956, **96**, 76.
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Special Articles

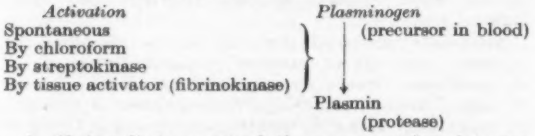
THE BIOLOGICAL SIGNIFICANCE OF FIBRINOLYSIS *

TAGE ASTRUP
D.Ph.
From the Biological Institute of the Carlsberg Foundation, Copenhagen, Denmark

FIBRINOLYSIS is the process by which the organism dissolves and removes deposits of fibrin. The development and the regulation of fibrinolytic activity in vivo are mediated through complicated reactions involving active, activatable, and activating, as well as inhibiting, agents. The mechanisms of these interactions are still not fully understood, but some light has been shed on some of the ways by which the organism regulates fibrinolysis and on the rôle of fibrinolysis in the development of certain pathological changes.

The Fibrinolytic System

The 1947 concept of fibrinolysis was as follows:



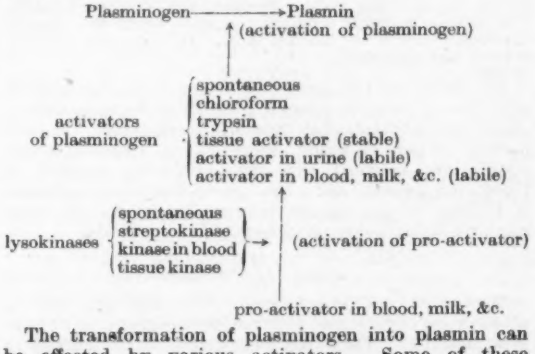
A fibrin-splitting proteolytic enzyme (plasmin) was produced from a precursor (plasminogen) in the blood. This activation occurred sometimes spontaneously and could be produced artificially by shaking with chloroform. In both cases the mechanism was unknown, though it had been found that the chloroform destroyed the inhibitors. Metabolic products (streptokinase) from certain strains of hæmolytic streptococci could also activate fibrinolysis, especially in man. An excellent review of this phase in the history of fibrinolysis was given by Macfarlane and Biggs (1948).

So long as the mechanism of apparently spontaneous fibrinolysis in vivo was obscure and no physiological activator was known, it was impossible to understand the rôle of fibrinolysis in physiology and pathology. Macfarlane and his colleagues were the first to study in detail the development of fibrinolytic activity in vivo. One of their most important findings was that fibrinolytic activity could be artificially produced in man by instituting conditions of stress and by injecting adrenaline. The underlying mechanism was, however, still obscure because adrenaline was ineffective in vitro.

At that time P. M. Permin and I were looking for the physiological activator of fibrinolysis. In view of the interaction of blood-proteins and tissue compounds in blood-coagulation we sought the activating principle in animal tissue and found in the water-insoluble proteins of several tissues a potent activator of plasminogen (Astrup and Permin 1947). This activator we called "fibrinokinase." Our finding was soon confirmed by Tagnon and Petermann (1949) and Lewis and Ferguson (1950) in America.

For these investigations we developed a new technique which approached conditions obtained in vivo. The lytic effect was estimated as the lysed area produced on a layer of fibrin clotted in a petri dish by placing tissue samples or drops of active solutions on top of the fibrin layer. The bovine fibrin used was found to contain large amounts of plasminogen. This finding immediately opened up a large question, because streptokinase had almost no effect on bovine blood or fibrin. One of the main objects of our research has since been to explain the discrepancy between the effects of the tissue activator and those of streptokinase. Of great help in the investigations was a further development of the estimation method consisting in denaturation of the plasminogen by heat. In this way we were able to distinguish between the effects of a true fibrinolytic enzyme and those of activators of plasminogen.

The investigations led in 1954 to a new concept of the activation of the fibrinolytic system in vivo as follows (Astrup 1956):



The transformation of plasminogen into plasmin can be effected by various activators. Some of these apparently have a catalytic effect (acting as specific plasminogenases), whereas others act through a stoicheiometrical reaction. Trypsin is the only proteolytic enzyme which transforms plasminogen into plasmin, probably by an enzymatic reaction. Plasmin cannot activate plasminogen, and the activation is not autocatalytic, as has been suggested. The tissue activator, which is a fairly stable compound, reacts probably by a stoicheiometrical reaction. The fibrinolytic activity found in normal urine (and in some other body-fluids) is caused by an activator of plasminogen, as in spontaneously active human blood.

Normal human blood contains, in addition to plasminogen, large amounts of a precursor of the plasminogen activator (a pro-activator). The transformation of this precursor into the activator may occur spontaneously but can be produced artificially by adding streptokinase. Streptokinase cannot directly transform plasminogen into plasmin. Agents effecting the activation of the pro-activator into plasminogen activator have been classified as lysokinases. Sometimes fibrinolytically active blood and certain tissues contain small amounts of compounds acting as lysokinases, but a potent source of the physiological lysokinase has still to be found.

In vivo the lytic processes are regulated by inhibitors (antiplasmin, antitrypsin), the amounts of which are especially large in the blood and in certain organs. The presence of these inhibitors interferes also with the estimation of fibrinolytic activity. In contrast to other proteases, plasmin and activating agents are adsorbed on to fibrin. By this mechanism plasmin exerts a specific effect on fibrin, and the interactions explain why fibrin has been the preferred substrate in studies of the blood-protease. The interaction with inhibitors plays a large rôle in vivo; it prevents the splitting of soluble proteins, including fibrinogen in the blood, though an effect is still exerted on fibrin. We can but admire the ingenious way Nature has solved the extremely difficult problem of providing blood with a proteolytic system which exerts its effect only when and where it is needed.

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Physiology of Fibrinolysis

Fibrinolysis is evidently a fundamental physiological process. So far two mechanisms for producing fibrinolytic activity are available for the organism:

(1) One process consists in the interaction between plasminogen and an activator released from injured tissue. This activator is rather thermostable, acts probably by a stoicheiometrical process, and is chiefly bound to the insoluble tissue proteins. This activation is therefore a process of primarily local significance.

(2) In the second process a pro-activator in the blood is changed into an activator of plasminogen. This activator is a soluble compound which is very labile and acts by an enzymatic reaction. It is carried with the blood-stream to all the organs of the body. Therefore the process is general. This process is highly significant in man, where the content of pro-activator in the blood is large. In most other animals it is of less importance.

The basic concept presented above of the fibrinolytic processes in vivo has made it possible to begin to understand the physiological rôle of fibrinolysis. In the normal living organism there exists apparently an equilibrium between the fibrin-producing process of blood-coagulation and the fibrin-dissolving process. A shifting in the balance between these two processes can lead to pathological changes (Astrup 1956).

SHOCK AND STRESS

Macfarlane and Biggs (1946, 1948) first suggested a relation between stress and the development of fibrinolytic activity. They observed increased fibrinolysis in anxiety, after heavy muscular work, and after the injection of adrenaline. In immune reactions—e.g., anaphylactic shock and peptone shock—fibrinolytic activity is produced (Rocha e Silva and Teixeira 1946, Ungar 1953). The activity developed in human blood obtained after sudden death and after electroshock therapy was found by Müllertz (1953) to be due chiefly to an activator of plasminogen.

The human organism is probably very sensitive because of the high concentration of pro-activator in human blood. In this connection it is interesting to note the inability of the rabbit to produce fibrinolytic activity after the injection of adrenaline (Williams 1951). The agent produced by the injection of adrenaline is very labile (Truelove 1951, Fearnley et al. 1952). The process involved in the rapid production of fibrinolytic activity in shock and after the injection of adrenaline is therefore probably the general process mentioned above, by which a pro-activator is transformed into a labile activator. The mechanism of this physiological process and its rôle in the organism are still obscure.

HÆMORRHAGIC DIATHESES

Some hæmorrhagic diatheses are caused by circulating fibrinolytic agents. The clinical aspects of this disorder are discussed by Stefanini and Dameshek (1955). Two separate conditions can be distinguished:

(1) In one type the bleeding occurs suddenly and is usually fatal. This condition is seen in obstetrical cases and sometimes during or after a surgical operation. It indicates shock, and the fibrinolytic activity in the blood is very high and is caused by a plasminogen activator. In a case of fatal amniotic-fluid embolism there was a high level of activator in the blood (Albrechtsen et al. 1955).

(2) In the other type the course is more protracted, resembles a hæmorrhagic diathesis—e.g., petechiasis and purpura—and sometimes accompanies such disorders as prostatic carcinoma and leukæmia.

In the acute type the high fibrinolytic activity is usually accompanied by lack of, or a decreased content of, fibrinogen. In the protracted type the fibrinolytic activity is usually much lower and the fibrinogen content can be normal. This can be explained, as mentioned above, by the adsorption of active agents on to the fibrin and the effect of inhibitors. The administration of fibrinogen helps such patients.

Hypofibrinogenæmia has been dealt with in *The Lancet* (1956). It should be pointed out, however, that the true danger lies in the combination of hypofibrinogenæmia with fibrinolytic activity, and that the effect of giving fibrinogen is sometimes insufficient when high fibrinolytic activity is present, as in the case mentioned above.

THROMBOLYSIS

In the treatment of thrombo-embolism coagulation of the blood is retarded either by increasing the effect of the inhibitors by administering heparin, or by decreasing the latent potency of the clotting system by application of anticoagulants of the dicoumarol type. However, in the resolution of persisting thrombi these methods of treatment rely completely on the organisms' own thrombolytic processes. By increasing the effects of these an active thrombotherapy can be instituted. This approach has been made chiefly by American investigators who have been able to draw on the large amounts of human blood supplied by the American Red Cross organisation.

Artificially produced thrombi can be dissolved by injecting solutions of plasmin prepared by means of streptokinase. Such preparations have also been used in man (Tillett et al. 1955). Streptokinase is prepared by cultivating β-hæmolytic streptococci and is therefore of bacterial origin. Serious side-effects after the introduction of such preparations into the organism have been reported. We have therefore tried to use plasmin prepared by activation of human plasminogen with the activator found in human urine. These preparations contain only proteins of human origin. They can lyse artificial thrombi in rabbits (Storm 1956). However, in some cases we observed loosening of the venous thrombus, subsequent embolism, and eventual death of the animal. These results reveal in the treatment an inherent risk which, perhaps, is most pronounced in venous thrombosis and less so in arterial thrombosis. This danger must be given careful consideration before the therapy is applied to man.

FIBRINOLYSIS IN BODY-FLUIDS

The finding of high concentrations of a plasminogen-activator in normal urine suggested a physiological rôle in the removal of fibrin deposited in the urinary channels (Astrup and Sterndorff 1952). The obstruction of narrow excretory ducts is obviously serious; therefore the organism probably has a way of preventing it. This argument led to a search for fibrinolytic systems in various body-fluids, and it was found that different fluids have different fibrinolytic systems, indicating differences in formation and function. Normal urine contains a high concentration of labile activator of plasminogen, no activator precursor, and only traces of inhibitors (Astrup and Sterndorff 1955). Human milk contains various amounts of activator of plasminogen, large amounts of activator precursor, and no, or very small amounts of an inhibitor (Astrup and Sterndorff 1953). Human lacrimal fluid (Storm 1955) and saliva (Albrechtsen and Thaysen 1955) have a similar composition. The almost complete absence of inhibitor clearly distinguishes these fluids from blood, which always contains large amounts of inhibitors. Human seminal fluid contains an activator of plasminogen and the activator precursor (Von Kaulla and Shettles 1953, Lundquist et al. 1955) and some inhibitor (Astrup et al. 1956). Its composition is therefore nearer to that of spontaneously active human blood (Müllertz 1953). Human amniotic fluid is inactive but contains large

amounts of activator precursor and of inhibitor (Albrechtsen and Trolle 1955); in this it is more like normal human blood (Müllertz and Lassen 1953). The labile activator in blood has been studied in detail by Bidwell (1953) and Müllertz (1955, 1956).

We are now trying to complete our comparative investigation of the various fluids in man in the hope that it will help us to understand their formation and physiological significance. They all have in common the presence of, or the ability to form, a labile plasminogen activator. This is the process which apparently is involved in conditions of stress and shock, and it represents the general process mentioned above.

FIBRINOLYTIC ACTIVITY IN TISSUES

As already mentioned, the tissue activator is rather stable, especially in an acid medium (Astrup and Sterndorff 1956). This property can be used to separate it from the labile blood activator. Usually the tissue activator is bound to insoluble tissue-proteins, but a method has been devised for its quantitative extraction and estimation (Astrup and Albrechtsen 1956).

Investigations of the activator content in tissues have shown that the various organs can be grouped into those which have a high content of activator, those with a medium content, and those with no or a very low content (Albrechtsen 1956a). The group with a high content includes organs known to have a latent tendency to bleeding; hence a relation between certain types of hæmorrhage and an active fibrinolytic system is corroborated. This applies to the uterus, the prostate gland, the lung, the thyroid gland, and the adrenal glands. The prostate gland differs from other organs so far investigated in that it contains both stable and labile activators, the latter evidently being secreted (Astrup et al. 1956). The uterus has a high content of tissue activator. This is true for the myometrium as well as for the endometrium (Albrechtsen 1956b). Human decidual tissue and placenta normally contain no activator. The activity of the endometrium explains the finding that menstrual discharge contains an activator of the tissue type in addition to large amounts of the activator precursor in blood. Further it contains plasmin but no plasminogen, explaining the absence of clotted fibrin in normal menstrual blood (Albrechtsen 1956c).

FIBRINOLYSIS AND WOUND HEALING

The ubiquity of thromboplastic agents in the organism, the presence of fibrinogen in lymph, and the constant infliction of minute injuries in the normal organism indicate that the formation of fibrin deposits is a regular phenomenon in the healthy organism. The re-establishment of normal conditions therefore depends on the ultimate removal of these deposits. Apparently there exist in the sound organism processes by which the fibrin deposits are continuously removed. It is known that leucocytes are active in this respect, especially where the lesions contain foreign chemotactic compounds —e.g., bacterial proteins. In the case of aseptic lesions not contaminated by foreign matter the removal of fibrin depends chiefly on the fibrinolytic mechanism (Astrup 1955). In the layer of fibrin deposited on a tissue lesion regenerative processes take place. After a few hours leucocytes migrate into the deposit, followed by fibroblasts derived from resting connective-tissue cells. Dead tissue, dead bacteria, and dead leucocytes are removed by phagocytosis. The fibrin is dissolved. Collagenous fibrils are formed by the migrating fibroblasts, and after complete organisation true connective tissue is left which later shrinks. There may also be vascularisation with the formation of granulation tissue, and the surface may be covered by epithelial cells migrating from the edges of the wound.

If there is to be no excessive formation of connective tissue, the fibrin deposits must be dissolved before there is any extensive organisation of the fibrin substrate. Their resolution can be hastened by the early local application of fibrinolytic enzymes (trypsin, plasmin); but, if the fibrin substrate has become organised, treatment with fibrinolytic enzymes is of little value.

The potency of the fibrinolytic system is apparently of paramount significance in the healing of wounds and in the forming of connective tissue. If the fibrinolytic system is of low potency (owing to a decreased concentration of activating and active agents or an increased effect of inhibitors), the fibrin deposits are retained longer, and an increased ingrowth of fibroblasts is followed by excess formation of connective tissue. If it is of high potency, or the inhibitors are decreased, healing of the wound is delayed. The barrier against the cause of the lesion can be broken down, leading eventually to dissemination of an infection. As mentioned above, a hæmorrhagic diathesis may also develop. The pathogenicity of bacterial strains depends (among other properties) on their ability to invade the host organism. Thus hyaluronidase-producing strains spread very rapidly. Similarly it has been assumed that the common ability of streptococcal infections to spread in the human body is caused by the breaking down of barriers of fibrin by the fibrinolytic agent (streptokinase) produced by some streptococci. The more local effects of staphylococci are said to be caused by the clotting principle (coagulase) produced by some of these bacteria. However, some strains produce also a fibrinolytic agent (staphylokinase).

The rôle of fibrinolysis in wound healing can also be studied in tissue-cultures. It is an old observation that some types of cells liquefy the plasma-clot when cultivated in vitro. Fischer (1949) and Morgan and Parker (1949) showed that growth of the culture could be maintained when an antitryptic agent (the soy-bean inhibitor) was added to the medium in small amounts. This technique has since been used in the propagation of virus in tissue-cultures (Enders and Peebles 1954 and many others). In our opinion the activity of the fibrinolytic enzyme system in the body is a main factor in the regulation of connective-tissue formation in tissue repair (Astrup 1955).

FIBRINOLYSIS AND ARTERIOSCLEROSIS

Although an immense amount of work has been done on arteriosclerosis during the past century and much valuable information has been collected, the cause of arteriosclerosis remains a riddle. However, it is possible now to suggest the rôle of fibrinolysis in this process without going too far beyond the scope of present experimental evidence.

Duguid (1949, 1954, 1955) argues that parietal deposits of fibrin cause atherosclerosis, as Rokitansky suggested a century ago. Duguid's conclusions, based mainly on necropsy material, are very convincing and have been partially confirmed by Crawford and Levene (1952). According to Duguid atherosclerosis and hyaline arteriolosclerosis originate from mural deposits of fibrin which become covered by endothelium and thus incorporated in the vessel wall and form, after subsequent organisation, fibrous thickenings of the intima.

We have reached a similar conclusion from more theoretical considerations, and we can support and even extend Duguid's theory. Mole (1948) first suggested a connection between fibrinolysis and Duguid's theory. We realise now that fibrinolysis is a fundamental physiological process and is not involved only in pathological states. In the healthy organism fibrinolysis is in a dynamic equilibrium with the fibrin-depositing coagulation process, and each of these two processes is regulated

by a multitude of activating and inhibitory systems. Concerning the rôle of fibrinolysis in arteriosclerosis our reasoning has been along the following lines:

As mentioned above, small amounts of fibrin are being constantly deposited because of the ubiquity of the thromboplastic agents and the latent activity of the coagulation process. In the healthy organism these deposits are removed by the fibrinolytic system as rapidly as they are formed. When the resolution is delayed, pathological processes can occur as described above.

Films of fibrin might also form on the walls of arteries, especially where strain causes tissue damage with local release of thromboplastic agents. In the sound organism these deposits apparently soon disappear, but in an organism with an unbalanced fibrinolytic system, where lysis is delayed, a sequence of serious events is initiated. The seriousness is caused by the special conditions prevailing in the arterial wall.

The central layers of the wall in the systemic arteries usually rely for their nutrition on the diffusion of oxygen and metabolic products to and from the arterial blood-stream. This applies to the intima as well as to the cells in the more central layers of the media. The vasa vasorum, which supply the external layers of the media, do not extend far enough to feed the more central layers, and the high oxygen-tension and the difference in blood-pressure make it possible for the cells to draw directly on an exchange with the arterial blood-stream for their nutrition. The formation of a film of fibrin on an arterial wall therefore not only represents the deposition of some inert material but also hinders the nutrition of the underlying layers of the wall. If this barrier is not rapidly removed by fibrinolysis the cells begin to die, producing necrosis and inducing regenerative processes. The very mobile endothelial cells will soon migrate in from the edges of the lesion, covering the deposit and restoring the integrity of the endothelial layer, as described by Duguid. They will be followed later by fibroblasts derived from the resting connective-tissue cells, and we have a process very similar to a normal wound healing. There is, however, a significant difference; the process in the arterial wall takes place in very poorly vascularised tissue. Consequently the fibrin deposit, before as well as after its organisation, hampers the diffusion of nutritive substances and metabolic products from the lumen to the cells in an adjacent area. In this critical zone there is a danger of necrosis, which is apt to spread. This makes the process in the arterial wall different from a similar process in tissues rich in capillaries. The metabolic disturbances are much smaller in such tissues.

It has been argued against Duguid's concept that it does not explain the common absence of atheroma after thrombosis in veins. The answer is that the walls of the veins are more highly vascularised than those of the arteries. The vasa vasorum may extend even into the intima, and the media is much thinner than in the arteries. The conditions in a vein therefore differ considerably from those in the arteries. A lesion can be vascularised much more rapidly, and only the most superficial cells depend on the blood-stream in the lumen for their nutrition. Therefore the lesion tends much less to spread. Furthermore venous blood has a higher fibrinolytic activity than has arterial blood. There are thus several good reasons for a relative lower frequency of phlebosclerosis than of arteriosclerosis.

Freshly formed fibrin is sticky. It plays a rôle in the agglutination of particles in the blood-stream, including the agglutination of platelets, as well as in phagocytosis. Freshly formed deposits of fibrin therefore easily take up particles, and in this manner lipid material might be collected. The infiltration of the fibrin deposits by lipid material will tend to decrease further the permeability for nutritive substances and metabolic products. In this manner the lipids accentuate the degenerative changes induced by the primary lesion in arteriosclerosis.

We have observed that the calcification that sometimes occurs in tissue-cultures is caused by an interaction between organic phosphates and phosphatases released from the cells, whereby insoluble calcium phosphate is deposited (Astrup and Henrichsen 1954). Alkaline phosphatase is released from the dying cells even if they do not contain free phosphatase in the living state. This applies also to fibroblasts derived from connective-tissue cells such as chicken-heart fibroblasts (Henrichsen 1956). In the necrotic areas in the arterial wall, therefore, alkaline phosphatase can be released and calcium phosphate deposited which can form the basis of a subsequent degenerative calcification.

Similarly the deposition of lipids in the intima can possibly be explained by an incorporation of lipid-containing fibrin deposits in the wall, followed eventually by a fatty degeneration of the necrotised tissue. This process is probably accentuated by the low degree of exchange, as mentioned above, but the cause of degenerative fat-formation has not yet been satisfactorily explained.

Conclusion

The problems dealt with here have been chosen to show how far the significance of fibrinolysis extends into the normal functions of the living organism. The results substantiate the concept of fibrinolysis as a fundamental physiological process. This concept has far-reaching consequences. It yields new and interesting aspects in widely divergent fields of physiology and pathology and provides us with new tools in the experimental approach of the causes underlying some important diseases.

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PHYSIQUE OF LONDON BUSMEN

EPIDEMIOLOGY OF UNIFORMS

J. N. MORRIS M.A. Glasg., M.R.C.P., D.P.H.
J. A. HEADY M.A. Oxfd
OF THE SOCIAL MEDICINE RESEARCH UNIT OF THE MEDICAL RESEARCH COUNCIL, LONDON HOSPITAL

P. A. B. RAFFLE M.D. Lond., D.P.H., D.I.H.
OF THE MEDICAL DEPARTMENT, LONDON TRANSPORT EXECUTIVE

IT has been shown[1] that in 1949–52 the "sudden death" rate and "three-month mortality" rate from coronary heart-disease were twice as great in the drivers of London buses as in the male conductors. On the basis of this observation, and other independent evidence, a hypothesis was stated that

> Men in physically active jobs have a lower incidence of coronary heart-disease in middle age than men in physically inactive jobs. More important, the disease is not so severe in physically active workers, tending to present first in them as angina pectoris and other relatively benign forms, and to have a smaller early case-fatality and a lower early mortality-rate.

In discussing this hypothesis[1 2] it was pointed out that the association observed might also be a reflection of other factors: for instance, there might be constitutional differences between drivers and conductors, and these differences might be a cause of the differences found in coronary heart-disease. One expression of constitution is body shape (though bodily measurements are, of course, also influenced by environmental factors); and, indeed, there is some evidence[3] that body shape is related to the development of coronary heart-disease—that square, muscular men, particularly if inclined to be fat, are prone. It is also clearly possible that drivers for instance, because of the sedentary nature of their work, might become more fat (whatever their somatotype), which might, again, render them more liable to coronary heart-disease. Thus there are already two aspects of physique of considerable interest in the study of coronary heart-disease.

It occurred to us that since drivers and conductors all had uniforms issued to them, and since these uniforms seemed on considerable personal observation to fit reasonably well, it might be possible by making a study of uniform sizes (i.e., an epidemiology of uniforms), rather simply and economically to obtain some idea of the physique of busmen. At the least, it might be possible to learn whether there were substantial differences in the size and shape of drivers and male conductors. The London Transport Executive kindly made available the sizes of the uniforms issued to drivers and conductors in three of their garages—two central bus (red, double-decker) garages and one trolleybus garage. The data relate to 1276 drivers and 994 conductors between the ages of 25 and 65, and to the year 1954.

Methods

Records are kept up to date when new uniforms are issued. The information available is the trouser-size and jacket-size for each man. From these sizes it is possible to deduce the measurements (height, waist, and breast) of men for whom the garments are made. Two words of caution are necessary here. These measurements are not of course exact measurements of the men to whom the garments are issued; nor, even if they were, would they be the measurements which would be made by a physical anthropologist or anthropometrist. They are tailors' measurements and make an allowance for comfort and slackness of fit. Thus, a different waist measurement might well be returned when a man is measured for his jacket compared with the one used for his trousers. With these points in mind, the waist measurement used in what follows is the measurement obtained from the trouser size, and the breast measurement that obtained from the jacket size. It was assumed that a man would reject a pair of trousers unless they fitted reasonably at the waist, or a jacket unless it was roughly right across the shoulders and chest. With these provisos, therefore, the data in the table are presented, bearing in mind that there is a good range of sizes available and that the points raised do not affect comparisons *between* drivers and conductors. It is not the practice, for instance, to give a driver a more loosely fitting jacket than a conductor of the same size on account of the arm movements involved in his job, or roomier trousers because he is chairborne.

Results

The table compares the drivers and conductors in two different ways—the percentage of the men (within a stated range of ages) who have a waist measurement of 36 in. or more, and the percentage who have a breast measurement of 40 in. or more. Drivers tend to be taller than conductors, partly because a maximum height of 6 ft. (until recently it was 5 ft. 11 in.) is prescribed for conductors, with no corresponding limitation for drivers; the rates are therefore "adjusted" to take this into account. (The method is described in the footnote to the table.)

Three points emerge:

1. The men's girth increases with age in both occupations (except, curiously, for drivers in the oldest age-group).
2. The girth of drivers is greater than that of conductors.
3. The difference between drivers and conductors is present at every age, even the youngest; and the difference is just as clear at 25–29 as at 55–59.

The first point calls for no comment, but is the reason for presenting the percentages at each age. Because the percentages are adjusted for height it can be said that the differences are present independently of age, and of height; in fact, more detailed analysis shows that they are present at each height, and each age.

The result of interest is that, on the average, drivers measure more round the chest and round the waist than conductors (the mean differences in both measurements varied from about 1 in. at age 30 to about 2 in. at age 60); and, more particularly, that the difference, amongst present-day drivers and conductors at least, is present even amongst the youngest of them. In other words, drivers are bigger even when they join the service. Since

WAIST AND CHEST MEASUREMENTS OF UNIFORMS OF DRIVERS AND MEN CONDUCTORS (LONDON TRANSPORT EXECUTIVE, 1954)

Age (years)	No. of men		% with trouser waist of 36 in. or more*		% with jacket breast of 40 in. or more*	
	Drivers	Conductors	Drivers	Conductors	Drivers	Conductors
25–29	67	168	7·9	3·4	10·5	4·7
30–34	168	162	19·1	9·2	14·4	10·2
35–39	165	134	21·7	13·3	18·8	10·1
40–44	197	165	30·7	17·4	21·0	14·0
45–49	214	121	39·7	22·7	33·4	17·8
50–54	185	99	51·0	32·6	42·2	21·3
55–59	160	87	63·2	42·0	50·8	25·5
60–64	120	58	57·9	45·3	44·6	34·7
Total 25–64	1276	994	..	..	..	..

* Adjusted to take height into account, using, at each age, the weighted sum of percentages in three height groups. The weights were the proportions of men in these three height groups in a "standard" population (drivers and conductors, combined, of all ages).
"Age" is age attained in 1954.
These men constitute the total "population" aged 25–64 of three garages (with the exception of one man whose uniform sizes were not recorded).

1. Morris, J. N., Heady, J. A., Raffle, P. A. B., Roberts, C. G., Parks, J. W. *Lancet*, 1953, ii, 1053, 1111.
2. Morris, J. N., Raffle, P. A. B. *Brit. J. industr. Med.* 1954, **11**, 260.
3. Gertler, M. M., White, P. D. Coronary Heart Disease in Young Adults. Cambridge, Mass., 1954.

it is unlikely that differences at 25–29 years of age are to any important degree the *results* of occupation, it may be postulated that the men have brought these differences into the jobs with them. The differences may be constitutional, or they may reflect previous environmental experiences, or both. In terms of nutrition [4] it is interesting that the ratio of the measurements inside-leg/height are the same in both occupations.

Comment

It remains, of course, to show whether or not the difference between the shape of the men in the two jobs is of the right kind and amount appreciably to affect their liability to sudden death from coronary heart-disease and other rapidly fatal infarction. (For various reasons the study must be limited to deaths.) Such a demonstration involves two stages: (*a*) to establish a relationship between waist and/or breast measurement and mortality from coronary heart-disease; (*b*) later, to ascertain from the distribution of these measurements in drivers and conductors, suffering and not suffering from the disease, whether the differences in girth do or do not explain an important part of the difference in mortality between the two jobs.

Data are not yet sufficient for a clear judgment on (*a*): the number of deaths from coronary heart-disease for which uniform measurements are available is too small, and is not likely to be big enough for some years yet; and the "scatter" of the uniform sizes is too great. We felt, however, that the information given in the table would be of interest, both for its own sake and as a demonstration of a method which might be used in a wide variety of different circumstances and problems.

It is a method which surmounts a number of practical difficulties. For the men with coronary heart-disease it gives information which was obtained *before* they were attacked. For the sudden deaths, which form so high a proportion of all deaths in this condition, this is vital because, for them, it is clearly impracticable to obtain the necessary measurements *after* the onset of the first attack. Moreover it gives data about a *complete population* without the necessity for measuring each individual specially for the investigation—an uneconomic procedure here considering the flimsiness of the hypothesis under test. This complete coverage thus serves two purposes. It ensures that there are data available for any man who is attacked; and, it provides data for the population at risk. In the present instance three samples of the population were analysed, and, because of their remarkable consistency, were accepted as representative of the whole; but the entire population—or any size of sample—could have been taken. The present interim report is, therefore, an example of how data which are admittedly crude, may, because of their accessibility on the one hand, and their regularity on the other, nevertheless clearly indicate differences.

Finally, it can be stated that, in a preliminary sample from one garage, separate analysis for men who joined the service as drivers, and for others who began as conductors and transferred later to driving, shows no consistent difference between drivers who have been conductors, compared with those who have not. Drivers in both groups are bigger than conductors, even at ages 25–34. This suggests that the conductors who become drivers are from the outset more like drivers in build. The finding, however, needs confirmation from larger numbers, and data from the remaining garages will be examined and presented in the later report.

We are very grateful to our colleagues in the London Transport Executive, particularly Dr. L. G. Norman, Mr. F. H. Spratling, Mr. K. G. Murden, and Mr. C. J. Cornwall, and in the Social Medicine Research Unit, particularly Mrs. V. P. Hall (computer) for much help.

4. Leitch, I. *Brit. J. Nutrit.* 1951, **5**, 142.

In England Now

A Running Commentary by Peripatetic Correspondents

THE highlight of my trip to Copenhagen was my visit to the Blegdam Hospital. There I saw some 20-odd patients with complete respiratory paralysis—the remaining casualties of the devastating polio epidemic of three years ago. At first glimpse it looked like a deep-sea diving establishment: the room pulsed with the hissing and sighing of pumps, from each of which an air-line went to a patient. But unlike the divers the patients did not wear helmets; instead the air-tubes ended in tracheotomy cannulæ, fitting snugly and tightly inside a human windpipe. Otherwise the patients were entirely free, untrammelled by box or cuirass.

Their comfort has to be seen to be believed. Nursing is easy, with complete access to the whole patient, and without the distress caused by opening the usual tank-respirator. The patients are mobile. They can be moved about in a wheeled chair. A small pump has been devised which attaches to the back of the chair, worked by a compressed-air cylinder slung under the seat. On this, patients can be taken for "walks" through the streets or carried on trains so that all of them have been able to spend weekends with their families. Many of them have learned to phonate a few words during the inspiratory (positive-pressure) phase; it is virtually the pharyngeal speech of the laryngectomised. All of them have most severe peripheral paralysis also, so that the only useful movement left may be head-movements, or a tiny flick of one wrist. Much ingenuity has been shown in exploiting such residual power—for example, most of them can manipulate an electric typewriter, tapping the keys with a stick held between the teeth.

The Danish government is offering free immunisation against polio to all below the age of 40; it is not surprising that the acceptance-rate is over 97%.

* * *

Once again we were at the central Wales farm where if lucky (we're not) one may see kites wheeling, and if unlucky (we are) receive more than one's fair share of rain. The one fine day saw us all busy hay-making, for though mechanisation is creeping steadily up the hillside there is still plenty to be done by hand. By 7 P.M. the hay which had weathered in tidy heaps the rain of the last few days had been spread out, turned, and was nicely dry and ready for carrying. It was then that the tractor broke down—the magneto, we soon discovered. A hurried conference resulted in a 10-mile dash by car into the market town, the garage-owner was rounded up, and we were back with a new magneto by 9 P.M., too late for the inexperienced to fit in the fast fading light. But we were not too late to hear that rain was spreading, so after a quick bite we were out in the field remaking the tidy, weatherproof hay piles. Tom in the farm above had also been listening to the weather forecast for he too reappeared and took in another load. By 10 P.M. we had finished and were retiring for the night when a shadowy form came to meet us as we strolled sadly back; it was Tom. Our bad luck was explained, and Tom said he'd be back with his tractor once he'd got his load into the barn and had some supper. We started loading at 11 P.M. by the aid of starlight and torch, and by midnight our hay was safely under cover.

The rain arrived before dawn with a gale of wind, and we had all day in which to fit the magneto in the shelter of a Dutch barn.

* * *

I was dozing in my seat aboard an airliner over the Atlantic when my companion nudged me sharply in the ribs. "Wake up! Doc," he said, "I think you are wanted back there." All the passengers were looking towards the rear of the aircraft. There I saw the air-hostess, who was holding a baby upside-down by its legs and slapping it smartly with her other hand. The baby's skin was cyanotic but as I came up it gave a weak cry and its colour immediately improved. It had apparently stopped breathing and had gone blue while lying in its

mother's arms. The distraught mother, very young and travelling alone, told us that it was her first baby and her first flight. She had travelled a long distance overnight before boarding the aircraft and the infant's feeding schedule had obviously been upset by the journey. I tried to examine the baby, which was a puny little thing only a few months old. Our aircraft was one of the more noisy types and, try as I would, I could hear nothing of what went on inside the infant's chest. However, its colour was then quite good and it was breathing regularly if rather shallowly. It seemed more tired than anything else and fell asleep as I was looking at it. I was reasonably happy that nothing much was wrong and I tried to reassure the mother as I handed the baby back to her. She accepted it unwillingly and stared at it as if it were some changeling. She could not convince herself that the child was indeed breathing, and within minutes her anxiety made her again cry out hysterically for the air-hostess. The latter, a most competent girl with a nursing qualification, then held the baby for a while, but she had many other jobs to do and could not nurse it indefinitely. The mother was obviously much too scared to look after it and the other female passengers regarded it somewhat askance. There seemed no alternative, so I took the child in my arms, much to the amusement of the other passengers, who were prepared to see the humorous side of the affair so long as it didn't involve them.

For the next four hours either the air-hostess or I held the baby. It stayed pale and listless but gave no real anxiety. I made two attempts to palm it off on a motherly looking passenger but she wasn't having any. The mother and baby were supposed to continue their journey to Western Canada by another aircraft soon after our arrival in Montreal, and in the circumstances I felt that the baby should be properly examined under quiet conditions to see if it was fit to continue the journey. I asked the captain to radio ahead to Dorval and arrange for the airport doctor to meet the aircraft.

As we came to a halt on the apron and the engines stopped there was an unusually prolonged silence. No-one seemed anxious to wheel the steps over to us, and the normally bustling officials hung back at a distance. I had reckoned without the quarantine regulations, and we were treated as outcasts until the airport doctor came to find out just what frightful illness we had on board.

The unaccustomed silence woke the baby, who stirred in my arms. It smiled for the first time, and I could have sworn that it winked at me as if to say "That *was* fun! didn't I fool them?"

* * *

As the tram-car fibrillated its way along the High Street I stole another glance at the pair sitting opposite me. The mother, tight-lipped and forbidding, stared fixedly into space. By her side, completely enveloped from head to waist in a large pillow-case, sat a small child.

Davy Crockett had, I knew, been consigned to the limbo of yesterday's heroes; space men were, on the authority of my youngest, quite *outré*. What this latest costume was meant to resemble I couldn't diagnose—the Klu Klux Klan, perhaps. A grimy hand tugged at the mother's dress. "Are we there yet, Ma?" a plaintive voice wailed. No reply was forthcoming and the voice trailed off into a dismal silence. Ghost riders of the sky, I thought, or Roy Rogers in disguise.

I rose as we came to our infirmary and at the same time the little figure was jerked upright and hustled off the tram. The conductress didn't look twice—the infirmary run was her regular route. As I walked up the drive I saw them ahead of me disappearing into the casualty entrance.

By chance I was called there a short time later. The mother stood grimly over a small boy, now divested of his costume while a perspiring house-surgeon and a nurse pulled and tugged. As a utensil it had its uses, but headgear was certainly not one of them. "He was playing at soldiers," said the mother not without a certain sombre satisfaction.

* * *

News from school.—My weight is 6 stone 6, my height is 4 foot 9; I have very good eyesight and very good earshot.

Letters to the Editor

THE MORTALITY OF ANÆSTHESIA

SIR,—It is easy to point out to Dr. Dunderdale (Sept. 1) that he need not be surprised that he has "never seen one obstetric case die as the result of the anæsthetic." I have produced evidence [1] which suggests that in England and Wales the frequency of death from this cause in obstetrics is of the order of 1 for every 30,000 births. There is, therefore, a tendency to dismiss the personal experience of any one general practitioner as of little value in this respect, since the sum-total of an average doctor's obstetric cases may not reach four figures in a life-time. However, the combined experience of numerous practitioners cannot be neglected.

I have been allowed to study the records of maternal deaths in recent years in Birmingham and have shown that no death due to anæsthesia occurred in a series of 100,000 confinements (including 3048 forceps deliveries) conducted at home. There is no reason to doubt the accuracy of this. Deaths associated with childbirth do not go unrecorded, and the few deaths which did occur in the home were certainly not due to the anæsthetic. Since, during the same period, there were at least 8 deaths due to aspiration in hospital, I came to regard hospital methods, and in particular the anæsthetic machine, with suspicion, and I continue to believe that avoidable maternal deaths occur owing to inexpert handling of the machine.

Until recently the open mask appeared blameless in respect of aspiration, but Lock and Greiss [2] record 4 cases, in a large series, in which fatal aspiration occurred during open-drop ether. It would be well therefore to keep an open mind, though Lock in a personal communication says: "Machines are often used by semi-skilled administrators, with more difficulty developing than when ether or chloroform is used by a complete amateur"—i.e., on an open mask.

Dr. Dunderdale implies that what we need today are "simpler and more direct methods in skilled hands." I prefer to leave "skilled hands" to choose the technique they prefer, but I would advocate the simple well-tried methods for the occasional anæsthetist. No shame need attach to the use of the open mask, if it gives the results I have quoted, in the home. Indeed I wonder if anything better (i.e., safer) can be taught to the student and houseman in hospital, provided he appreciates the dangers of chloroform. (Of the 29 deaths reviewed by Edwards et al.,[3] 2 were due to chloroform.) It may be assumed that he is already being taught the advantages of local anæsthesia over any other method, when it can be used.

Walsall. R. B. PARKER.

SPREAD OF ANTIBIOTIC-RESISTANT BACTERIA

SIR,—In your leading article of Aug. 11 you used the words "Doctors should think twice about using antibiotics at all in most cases in which they are now given."

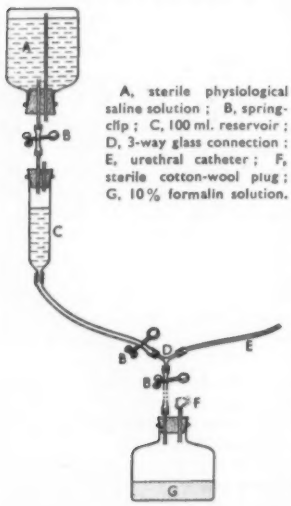
The fantastic cost of antibiotics to the National Health Service resulted at the end of 1955 in my deciding on an experiment at the Royal Northern Hospital. I issued instructions that in my firm no antibiotic should be prescribed without my permission, unless the registrar considered that the patient's life might be in danger by any delay in obtaining it. So far in 1956, antibiotics have been prescribed for my patients on three occasions only.

London, W.1. RAYMOND GREENE.

1. Parker, R. B. *Brit. med. J.* July 7, 1956, p. 16.
2. Lock, F. R., Greiss, F. C. *Amer. J. Obstet. Gynec.* 1955, **70**, 861.
3. Edwards, G., Morton, H. J. V., Pask, E. A., Wylie, W. D. *Anæsthesia*, 1956, **11**, 194.

PROSTATECTOMY AT HOSPITAL B

SIR,—Your leader of Aug. 18 was of great interest to those of us who work in hospital B. There are many reasons why our results are not as good as those of our colleagues in A. Shortage of nursing staff is one, and another is the inevitable mixing of cases that takes place in an unspecialised unit. A "clean" prostatectomy is not infrequently found in the next bed to a patient whose abdominal wound is discharging pus following the removal of a gangrenous appendix. I am sure that, under these circumstances, washing out the bladder is a common cause of cross-infection. It is at times anything but an aseptic procedure and should, ideally, be avoided altogether.



A, sterile physiological saline solution; B, spring-clip; C, 100 ml. reservoir; D, 3-way glass connection; E, urethral catheter; F, sterile cotton-wool plug; G, 10% formalin solution.

For some time now I have used, for cases requiring catheter drainage, the method described by Mr. E. W. Riches, whereby the catheter is connected to a bottle containing a strong solution of formaldehyde. The vapour from this solution keeps the interior of the drainage-tubing and catheter sterile. The system is never disconnected except to change the bottle. Cystitis and urethritis are, in comparison with other methods, amazingly reduced, and, in uncomplicated cases, bladder lavage is unnecessary.

Drainage of the bladder after prostatectomy is a more complicated problem. I must confess at once that I am not a surgeon in whose hands reactionary hæmorrhage "has not presented any problems."[1] Some of my cases require frequent bladder lavage in the first twenty-four hours after prostatectomy. If this is done with a syringe, with repeated laying up of a sterile trolley and disconnection of the drainage-tubing, infection is inevitable. I therefore use a modification of the bladder-irrigation apparatus devised by Dr. Cuthbert Dukes for use at St. Mark's Hospital. Physiological saline at room-temperature is used. Complete sterility of this solution is ensured if sealed bottles normally used for intravenous therapy are employed. The accompanying figure is self-explanatory. By manipulation of the spring-clips the bladder can be washed out very frequently without disconnecting the system, which is sterile to start with. The reservoir C is made to hold 100 ml., so that the amount of fluid run into the bladder is easily estimated and over-filling avoided. Rubber tubing of medium thickness is used, and, by "milking" this, small clots can be sucked out of the bladder with ease. Occasionally it has been necessary to clear the catheter with a bladder syringe, more particularly in cases with secondary hæmorrhage, but in general this method has now been abandoned.

Urine specimens taken from the catheter just before its removal and from the first amount passed naturally by the patient have, in more than three-quarters of cases, been sterile.

Neither of these techniques is original, but I have ventured to draw attention to them because they have greatly improved the results of prostatectomy in my hands, while at the same time the work of the nursing staff has been materially lightened.

Newmarket General Hospital. R. E. B. TAGART.

SIR,—I was much interested in the papers, in your issue of Aug. 18, by Mr. W. Skyrme Rees and Mr. P. Dawson-Edwards on the control of hæmorrhage after open prostatectomy. Although I am not competent to comment on the surgical procedures involved, I feel that some of the anatomical features of the arterial supply to the prostate[2] may be not without interest.

There are three main groups of arteries concerned in the supply of the gland—on either side the prostatic (or inferior vesical) arteries, and, more medially, the continuations of the two arteries to the vasa deferentia, which pass into the gland along the ejaculatory ducts. These latter vessels are of considerable size and supply the greater part of the urethral crest.

The prespermatic acini, where benign enlargement occurs, are supplied partly by vessels which run anteromedially and posteromedially between the bladder neck and the base of the prostate, and partly by vessels lying on the anterolateral surfaces of the gland. Both these sets of vessels would be torn in the enucleation of an adenoma, and better hæmostasis might be secured if the controlling sutures were placed at 3 o'clock and 9 o'clock rather than more posteriorly.

The vessels accompanying the ejaculatory ducts will also be liable to damage during the removal of an adenoma, and I think they are the cause of arterial bleeding from the depths of the cavity, when it occurs. The method used by Mr. Skyrme Rees would seem to arrest this bleeding by the pressure of the bladder neck on the posterior wall of the prostate cavity, where these vessels lie. The drawing down of the bladder neck would itself help to obstruct them.

Although it might be difficult in practice, another method of combating bleeding from these vessels might be to tie the vasa deferentia as close to the prostate as possible, since in the gland itself they have few anastomoses with neighbouring vessels.

Department of Anatomy, University of Liverpool. E. J. CLEGG.

PILONIDAL SINUS OF THE UMBILICUS

SIR,—Mr. Patey and Mr. Williams (Aug. 11) misquote me as saying that direction of hair growth may indicate a "congenital" origin. I have, in fact, studiously avoided this term because it would commit me to a lesion present at birth. The term much more appropriate to the circumstances is "developmental."

They pick the umbilicus as the site of "an undisputed acquired pilonidal sinus." To record a single case, in which no history of trauma is revealed, in confirmation of a theory dependent on trauma for its validity, leaves a vital gap unbridged. To select the umbilicus, a landmark of developmental turmoils, for the refutation of the developmental theory of pilonidal sinus, strikes one as rather odd.

If Mr. Patey and Mr. Williams wish to be believed in the scientific sense, they must show that:

(*a*) The hair inside the sinus resembles loose abdominal hair in all respects.

(*b*) Subclinical trauma occurs.

(*c*) Such trauma has either demonstrable causes of its own, or may result from loose abdominal hair.

(*d*) If the latter, blunt hair bulbs can demonstrably, under existing circumstances, penetrate intact or damaged skin.

(*e*) Blunt hair bulbs will progress to a considerable depth, not in ones or twos, but in tens or hundreds.

(*f*) During such progress they will remain perfectly parallel to each other.

(*g*) Apart from the surgeon's knife, there are no forces capable of disimpacting the hairs.

(*h*) This train of events, on the above evidence, can most usually be expected in hairy males of a certain age-group.

1. Dawson-Edwards, P. *Lancet*, Aug. 18, 1956, p. 332.

2. Clegg, E. J. *J. Anat., Lond.* 1955, **89**, 209.

I have only gone as far as (*a*). The perfect uniformity in appearance of the hair bulbs shown in Mr. Patey and Mr. Williams's article could not be equalled by random hairs found on the abdomen.

The only feasible conclusion is that their case was a developmental pilonidal sinus, to be classed amongst dermoids.

London, S.W.10. F. E. WEALE.

X RAYS AND LEUKÆMIA

SIR,—Dr. Alice Stewart and her colleagues are to be congratulated on their survey of malignant disease and leukæmia in childhood (Sept. 1), and, following their interim report, the final report will be awaited with great interest.

It is unfortunate, however, that your criticism of the two previous surveys mentioned in your leader—i.e., that the control groups were not entirely satisfactory—can be levelled at the Social Medicine survey also.

The indication for abdominal radiography of the pregnant woman may vary from place to place throughout the country, but it would be safe to say that diagnostic radiographic procedures must be far more common during the first than during subsequent pregnancies. Unless, therefore, the controls were matched according to whether the child is the first, second, or third, &c., with the "cases," a quite misleading set of figures on this relatively small number may be obtained.

Perhaps this factor has been taken into account in the selection of the controls, but this is not apparent from the preliminary communication. If, in fact, it has not been taken into account, perhaps this could be remedied, for it would be a great pity if this survey should only provide figures so easily open to debate.

If it can then be established without question that antenatal radiography is of importance in the ætiology of malignancy in childhood, then it would be of both fundamental and practical importance to see if there is any correlation between the time in pregnancy at which radiography is performed and the subsequent development of malignancy.

The Churchill Hospital, Oxford. FRANK ELLIS
CHARLES L. LEWIS.

**We showed this letter to Dr. Stewart and her reply follows.—ED. L.

SIR,—The cases and controls were matched for age, sex, and locality because these features of leukæmia and cancer were already known from national statistics. But they were deliberately *not* matched for birth rank. Had we done this we would inevitably have failed to discover what now seems to be the case—namely, that the child population dying of leukæmia and cancer nowadays includes a disproportionately large number of first-born children and twins. Dr. Ellis and Dr. Lewis may have noticed that in the preliminary report the number of abdominal X-ray examinations made *before* the relevant pregnancy was less for the survey group than for the controls. These include some barium meals, pyelograms, &c., taken before marriage, but I think the deficit is an indication that there will eventually prove to be more first-born children among those who died of leukæmia and cancer than would be expected if the children had a birth-rank distribution characteristic of a "normal" population of the same age, sex, and locality (i.e., of the control group as at present constituted).

Now I can think of no reason why, when first conceived, first-born children should be more likely to develop leukæmia or cancer than other children; but, as Dr. Ellis and Dr. Lewis have pointed out, abdominal X-ray examinations are made more frequently in the first than in subsequent pregnancies. In fact even had we failed to record antenatal use of X rays on the schedules, merely discovering that there were more primiparæ among the mothers of the survey children than among the mothers of the controls, ought to have made us realise that the X-ray histories might be relevant.

The point about the twins is that there are in the survey cases several children who were X-rayed in utero and whose twin brother or sister has survived. To me this fact suggests that where there is more than one fœtus the one that happens to be lying anteriorly when the X-ray examination is made is peculiarly vulnerable—not that twins have a hereditary susceptibility to cancer.

I am not at the moment in a position to quote parity figures for the mothers included in the preliminary report (I am away from Oxford in search of further coöperation from public-health departments); but Dr. Ellis and Dr. Lewis can rest assured that the numbers for the whole series will eventually be published.

As to the timing of the X rays, the exact dates and estimates of ionising radiation have still to be obtained. But since most of the photographing was done for twins, breeches, disproportion, and placenta prævia, most of the films were taken after the 30th week.

May I also mention a point raised in your very interesting leader of Sept. 1. You suggested that it would have been helpful if, in the table in our preliminary report, we had listed the number of mothers who were given sulphonamides during the relevant pregnancies. The reason why these were omitted is that in the whole set of 1094 mothers there were only 13 such cases—7 in the survey group and 6 in the controls.

ALICE STEWART.

THE BACTERIOLOGIST IN MEDICINE

SIR,—The answer to the query, "should a university-trained bacteriologist avoid medical bacteriology unless he possesses a medical degree?," posed in Mr. MacGarvie's letter last week, is "yes"—until there is instituted recognised grading as in the case of non-medical hospital biochemists. A non-medically-qualified individual can never take full part in clinical or pathological discussion, because of lack of training in the processes of medical thought, for clinical science lacks the precision of an exact science such as physics, or the lesser exactness of bacteriology. Academically qualified bacteriologists can, however, be excellent assistants, *not technicians*—as, for example, obtained in the International Health Division of the Rockefeller Foundation.

However, Mr. MacGarvie appears to have overlooked the fact that it is possible to receive academic training in bacteriology (in a science faculty) concurrently with a medical course.

I think that the Acute Respiratory Service at the Rockefeller Hospital under Avery was the ideal, for the medical bacteriologist had his own cases and carried out his own treatment, at the same time gathering a wealth of clinical, bacteriological, and immunological knowledge which it is difficult otherwise to get.

Department of Pathology, General Hospital, Northampton. R. M. HEGGIE.

DISMISSAL ON MEDICAL GROUNDS

SIR,—Dr. Todd (Sept. 1) has drawn attention to some ideas on medical examinations in industry which I had hoped were becoming obsolete. We have not been given the reasons which made the doctor at the National Dock Labour Board come to the conclusion (which was supported by a tribunal) that Mr. McKibbin should not continue as a labourer. If Mr. McKibbin works—as is likely—as a member of a team, his condition may jeopardise the safety of his team-mates particularly among the dangers of dock work (for example, we do not know the visual acuity in his remaining eye), and he may therefore fall into the same category as the epileptic bus-driver whom Dr. Todd would not allow to drive. We do not know the full facts, and it is unfortunate that Dr. Todd should publicly denounce a colleague on the basis of a newspaper report.

Those of us who devote our life's work to bringing our knowledge of medicine to the service of industry have often heard the views to which Dr. Todd has drawn attention; we spend a good deal of time in trying to overcome them.

The Association of Industrial Medical Officers is publishing a booklet this month entitled the Functions of an Occupational Health Service in an Industrial Organisation. I am sure that after reading it Dr. Todd will be convinced that we are entirely Hippocratic in our outlook and work. Our nation has much to gain if we doctors continue to bring high principles and technical resources to the service of industry. Shall we work together to this end?

London. L. G. NORMAN.

HOSPITAL TRAINING AS PREPARATION FOR GENERAL PRACTICE

SIR,—Dr. Hodgkin's figures (Aug. 25) confirm the impression that a large group of disorders dealt with in family practice are never seen in hospital. The remedy is certainly to introduce the undergraduate to general practice and this is better done, not in the ward round where the attendant general practitioner can merely talk about cases which aren't there to be demonstrated, but in the surgery and the home—natural environment of doctor and patient. In addition to seeing some of the 75% of disorders which never get to hospital he finds there a new aspect of medicine—illness in relation to the family—which will broaden his knowledge of and colour his thinking about the patients he sees in hospital. The earlier in the clinical course this introduction is effected the better.

For some years I have been one of several general practitioners introducing first-clinical-year students to general practice. They sit in on our surgeries and come out on our rounds. My impression is that the experience has neither muddled them nor been regarded as an irrelevant extra, but has shown them what a satisfactory life general practice can be.

Newcastle upon Tyne. ANDREW SMITH.

PRIMARY ALDOSTERONISM

SIR,—In answer to Dr. Jacobides's remarks (Sept. 1) we would like to make the following points.

The boy was indeed small for his age, he had hypogonadism, his bone age was 13 years, and there was no axillary hair and little pubic hair. According to Dr. Jacobides, these abnormalities indicate "some pituitary dysfunction." In our paper, however, we mentioned that aldosterone production showed a marked increase (excretion 34 µg. in 24 hours), while no indications were found which could suggest still another abnormality of the adrenal cortex, for the patient had a normal excretion of 17-ketosteroids with a normal differentiation (Dr. Huis in't Veld) and normal levels of 17-hydroxycorticoids, of pregnandiol, and of gonadotrophins. The corticotrophin test was also normal. In the resected adrenals Dr. Wettstein found normal hydrocortisone and corticosterone levels.

It has been established that retardation of growth and development may be caused by potassium deficiency.[1–3] This may be related to the fact that potassium is required for the formation of cytoplasm. Patients with primary aldosteronism have a marked potassium depletion. It seems therefore probable that the physical signs are due to potassium depletion. The polyuria, polydipsia, and electrocardiographic abnormalities are also the result of lack of potassium.

The glucose-tolerance test does not show a "lag" curve. The levels did not exceed 180 mg. per 100 ml., but the fall was delayed. This curve may be explained by the combined effects of aldosterone and potassium depletion on carbohydrate metabolism. This point will be elaborated in a paper to be published in the *Acta Endocrinologica*.

In hypopituitarism the zona glomerulosa may be markedly atrophic. In one case we found only small fragments of the zona glomerulosa, but the zona fasciculata though more narrow than usual was much better preserved.[4]

A case of pituitary dwarfism showed a considerable reduction of the zona glomerulosa. The zona fasciculata while narrow was definitely less changed.[5]

"Crises" due to disturbances of the electrolyte metabolism may occur in hypopituitarism.

In our patient hyperplasia of the zona fasciculata was the predominant feature. In Conn's photomicrograph[6] the cells of the adenoma showed a pattern closely resembling that found by us in the hyperplastic zona fasciculata. It is therefore highly probable that the cells in the zona fasciculata are concerned with the production of aldosterone.

F. S. P. VAN BUCHEM
H. DOORENBOS
Groningen, Holland. H. S. ELINGS.

1. Grijns, G. *Z. Physiol. Chem.* 1938, **251**, 97.
2. Brokaw, A. *Amer. J. Physiol.* 1953, **172**, 333.
3. Offerijns, F. G. J. Thesis, University of Amsterdam, 1955.
4. van Buchem, F. S. P. *Acta endocr., Copenhagen*, 1955, **19**, 165.
5. van Buchem, F. S. P., Arends, A. *Acta med. scand.* 1955, **152**, 81.
6. Conn, J. W., Lawrence, H. L. *Ann. intern. Med.* 1956, **44**, 1.

THROMBOSIS OF THE SIGMOID SINUS

SIR,—In the modern world, and especially in the more developed countries, thrombosis of the sigmoid sinus as a complication of aural suppuration is rare. Mr. Reading and Mr. Schurr's article last week is thus, as they say, an obituary, but its conclusion should not, even in an obituary, pass without comment. I have discussed elsewhere[7] certain principles of the pathology of this condition, and, as all the sources quoted by Mr. Reading and Mr. Schurr are of earlier date, I offer a brief recapitulation of these principles as a supplementary obituary notice.

Sinus thrombosis was at one time the commonest intracranial complication of aural infection. It occurs during the course of acute, suppurative (and usually coalescent) mastoiditis, and also in acute exacerbations of chronic mastoiditis. As the former type of infection has virtually disappeared, the latter is the origin of nearly all the cases occurring nowadays (as well as, incidentally, of nearly all other intracranial complications).

Thrombosis is the natural reaction of a blood-vessel to injury, and is a specific instance of the pathology of inflammation and repair. If the blood-vessel is ligated in continuity beyond the thrombus, or if a portion of the vessel is resected, thrombi will again form at the points of surgical intervention. It is thus impossible to remove all clot, as it inevitably re-forms after the act of removal. In the absence of infection a thrombus is firm and tenacious and adherent to the walls of the vessel. Occasionally pieces may be swept away and cause remote embolism, an unfortunate imperfection in the defence mechanism, nothing in Nature being absolutely perfect; but generally speaking the mechanism works admirably. Aseptic infarction of any magnitude resulting from lateral-sinus thrombosis is almost unknown, and can be ignored for all practical purposes. The danger lies in the thrombus becoming infected and therefore friable, and in the dissemination of fragments of clot containing pathogenic bacteria. This was first described in 1880 by Zaufal,[8] who advised treatment by opening up the sinus, evacuating any septic clot, and sometimes ligating the internal jugular vein. The surgeon's knife was in his day his only weapon, and he was also probably dealing with virulent types of infection which are now rare.

The two principles of modern treatment are to remove the source of infection, by mastoidectomy, and to sterilise the clot, thus either preventing embolism, or at any rate ensuring that the emboli are not infected. Chemotherapy is the weapon of choice in applying this second principle, for it can penetrate more deeply than any surgeon's knife. Only when chemotherapy has demonstrably failed to control the pyæmia or bacteriæmia is surgical interference with the sinus justifiable or necessary. In such a case the clot has probably already

7. Ellis, M. *In* Modern Trends in Diseases of the Ear, Nose and Throat. Edited by M. Ellis. London, 1954; p. 177.
8. Zaufal, E. *Prag. med. Wschr.* 1880, **5**, 516.

broken down and is becoming liquefied and purulent, and the object then is not so much the removal of a clot (and the production of another!) as the drainage of an abscess. This method of approach is accepted in the treatment of cavernous-sinus thrombosis, and should be equally applied to lateral-sinus thrombosis.

The focus of infection in the bone having been removed, and the infection in the sinus controlled (or drained), further surgery is unnecessary. Tying the internal jugular vein, or resecting a part of it, is redundant, since the blood-stream is no longer being fed with organisms, and those already present in it can be eliminated by the appropriate antibiotics. In the past twelve years I have seldom opened the lateral sinus, and I have never yet (even in the years 1937–40) interfered with the internal jugular vein. My mortality-rate in this period is the same as Mr. Reading's. I have a great respect for his opinions, but, for the reasons given above, I cannot accept that operations on the sinus and the internal jugular vein as a routine treatment of sinus thrombosis is the right modern approach.

London, W.1. MAXWELL ELLIS.

RENAL TUBULAR ACTIVITY

SIR,—Dr. Nordin and I are grateful to Dr. Dowdle, Dr. Jackson, and Dr. Hoffenberg (Sept. 1) for drawing attention to the difficulty of deriving for clinical purposes, an index of renal tubular activity with regard to phosphate (P). Simultaneous measurements of urine and plasma concentrations cannot easily be interpreted. We had included in our table I, merely as one of several items of evidence for our patients' osteomalacia, the values for the Cp/Ccr (the ratio of the clearance of phosphate to that of creatinine) and the plasma-P concentration. Since all these Cp/Ccr values were abnormally high in association with abnormally low serum-P levels, we believe that these do indicate that these patients showed a low renal threshold for P; such as might be caused by the secondary hyperparathyroidism of osteomalacia. For brevity, we did not discuss this supportive evidence.

Clearly a single Cp/Ccr measurement merely indexes the proportion of P filtered by the glomerulus which passes on into the urine, or is not reabsorbed by the tubules. As we have noted in the references cited,[1] this Cp/Ccr, or the unreabsorbed fraction, rises and falls with serum-P levels, apart from any changes in renal tubular function. Thus, as Dr. Dowdle and his colleagues have noted, the Cp/Ccr value must be assessed against the range of normal Cp/Ccr values to be expected with the correlated plasma-P concentration. This may be done against a graph [2] or, in the normal and lower ranges of plasma-P, by calculating a "phosphate excretion index" described below.[3]

Dowdle, Jackson, and Hoffenberg have suggested, as an alternative index of the renal tubular handling of P, the determination of the mean P threshold by Tm_p procedures. This procedure is satisfactory for high serum-P levels, such as those induced by P infusions.[4 5] But, as these authors also show, the normal and lower P levels do not involve the full Tm reabsorption. Hence at normal or lower levels of serum-P, the calculation of the mean threshold by Tm procedures will obviously underestimate the mean threshold to an extent varying with the serum-P level. The "phosphate excretion index" procedure which we have suggested [3] is not a perfect index (since the straight-line relationship on which it is based is really slightly curvilinear); but it is of practical value in the range of serum-P values encountered clinically. This index measures the deviation of the observed Cp/Ccr from the normal range expected at that serum-P value as follows:

"Phosphate excretion index" = Cp/Ccr $-0{\cdot}05\ p + 0{\cdot}05$ (normal $= 0 \pm 0{\cdot}12$) (p=serum P in mg. per 100 ml.).

This index becomes unsatisfactory (and is unnecessary clinically) with serum-P values above 6 mg. per 100 ml., where however Tm procedures are applicable instead.

Postgraduate Medical School, Ducane Road, London, W.12. RUSSELL FRASER.

1. Nordin, B. E. C., Fraser, R. *Clin. Sci.* 1954, **13**, 477.
2. Milne, M. D., Stanbury, S. W., Thomson, A. E. *Quart. J. Med.* 1952, **21**, 61.
3. Nordin, B. E. C., Fraser, R. Ciba Foundation Symposium on Bone Structure and Metabolism. London, 1956; p. 222.
4. Longson, D., Mills, J. N., Thomas, S., Yates, P. A. *J. Physiol.* 1956, **131**, 555.
5. Anderson, J. *Ibid*, 1955, **130**, 268.

THE FINAL EXAMINATION

SIR,—Sir John Conybeare, in his letter last week, judged the diagnosis in Professor Bull's model to be hypoglycæmia. Myself I plumped for subarachnoid hæmorrhage, suspecting that an occasional stiff neck in Ulster might escape comment. A preregistration house-physician and I both agreed that an examiner who expected the examinee to differentiate between hypoglycæmic and hyperglycæmic coma, without mention of air-hunger, could not himself achieve an honours mark.

I think these multiple-choice questions may have a useful, though limited, place in the final examination. They may be used to test factual knowledge and, in a lesser degree, deductive power. The same group of mental qualities is assessed by them as is employed in the solution of a crossword puzzle. They cannot be used to test clinical judgment, nor are they a safe and complete guide to the student's intellectual capacity. A recent experience convinced me that students who appear to be of average quality when judged by other tests may do either very well or very badly in their answers to these multiple-choice questions.

I must confess to a personal bias against this method of examination in medicine. I remember too well my discomfiture at my final score in such a test in a Boston hospital at eight o'clock in the morning.

It may be this bias which makes me regard this method of examination as alien from the science of medicine and hostile to its art; just as the famous question in the English paper destroyed the spirit of poetry:

"O cuckoo, shall I call thee bird or but a wandering voice? State the one to be preferred. Give reasons for your choice."

It may be bias again which makes me see these tests as giving an undue importance to lowly, if essential, mental aptitudes; as did this question addressed to the "11+" children: "Of what does the following sequence of letters remind you, OTTFFS?" Examiners must surely seek additional ways of disguising their deficiencies.

Derby. DOUGLAS HUBBLE.

SHORTAGE OF MIDWIVES

SIR,—I do not think that Mr. Terence Robinson (Sept. 8) will get very far with his scheme for meeting this shortage, since it is not to be expected that the Central Midwives Board will admit that its policy has been wrong for many years.

The nursing of women in childbirth may reasonably be included as a part of general nursing, but at the beginning of the century, when it was particularly urgent that something should be done to improve the midwifery service, the general nurses were not ready for organisation.

Accordingly the Central Midwives Board was established to look after a part of nursing. By the time

it became possible to organise general nursing the Central Midwives Board had become a very powerful body with a strong corporate sense. It was politically impossible to abolish it and hand over its functions to the General Nursing Council.

Specialisation was beginning to be the spirit of the age, and the rift between general nursing and midwifery was later widened by the College of Midwives which adopted certain mystical ideas on the subject, saying that since childbirth was a physiological process and not a disease midwives were different from and superior to general nurses, who were concerned with pathological processes.

For many years there was just one C.M.B. certificate and training did not cover two parts as at present. It was then usual, in general hospitals which had maternity departments, for almost all the student nurses to take the course in midwifery after obtaining a general certificate. This was a great administrative convenience and ensured an ample supply of midwives. However, many nurses who took the certificate did not in fact practice midwifery, and this caused much annoyance. I always felt that personal feeling rather than zeal for the nursing service was the motive for setting up two-part training.

One effect of the regulations is the shortage of midwives which is worrying Mr. Robinson.

Liverpool. HENRY H. MACWILLIAM.

TOO MUCH CAFFEINE ?

SIR,—I should like to draw attention to the appearance on the market of a new stimulant preparation called 'Pro-Plus,' advertised as the "new safe pep-up tablet." It is said to be without any side-effects and is recommended in doses of up to 12 tablets daily.

In fact, each tablet contains 50 mg. caffeine, so that the total daily dose might be something like 0·6 g. (gr. 10). The *Extra Pharmacopœia* (Martindale) gives the dose of caffeine as 0·3–0·6 g. and states that "doses of 1 g. or over may produce alarming symptoms including tachycardia, and even therapeutic doses may cause unpleasant side-effects."

The type of person who would take these tablets is likely to drink many cups of tea and coffee each day in addition, so that a total of 1 g. of caffeine might easily be ingested. I feel, therefore, that it is misleading for the manufacturers to state specifically "for teenagers Pro-Plus is quite harmless and without 'undesirable' effect," and insufficient for them merely to advise that it should not be given to very young children or "taken within 2 hours of bedtime because it is a stimulant."

Liverpool, 18. M. GOLDMAN.

*** We showed Dr. Goldman's letter to the manufacturers and their reply follows.—ED. L.

SIR,—It is misleading to compare the *single* therapeutic dose of Martindale (300–600 mg.) with the total *maximum* daily dose of 'Pro-Plus' which is taken over a period of 12 hours or more. The *normal* dose is one to three tablets—i.e., 50–150 mg.—approximately equivalent to one or two cups of tea or coffee. The quotation that "1 g. or over may produce alarming symptoms, including tachycardia" is therefore irrelevant in this context, since again the reference is to a single dose. One would have to ingest more than a complete pack of pro-plus tablets at one time to receive 1 g. of caffeine.

In actual fact, caffeine is one of few drugs which have an enviable record of safety. For example, Goodman and Gilman [1] state that "the toxic dose of caffeine for man is so large (over 10 grams) that no human fatalities have been reported." It is significant that tablets containing 64·8 mg. of caffeine (in conjunction with aspirin) have remained official in the *B.P.C.* for many years and have been freely obtainable.

In the interests of all concerned, every reputable manufacturer conducts exhaustive tests on a new product before it is released, however well known the therapeutic agent may be. Prior user tests indicated a complete absence of side-effects and subsequent experience in many thousands of cases has brought no hint that pro-plus is in any way harmful.

Ashe Laboratories Ltd., Leatherhead. L. L. F. DEADMAN, Director of Research.

1. Goodman, L. S., Gilman, A. Pharmacological Basis of Therapeutics. New York and London, 1955; p. 341.

EXPERIMENTS ON STUDENTS

SIR,—At last you emphasise, in your annotation of Aug. 25, that "there are other problems raised by the use of healthy medical students. The results may not be the same as in ill patients." If this is true of humans how much more does it apply to healthy animals which differ greatly according to species and also to their physiological make-up. Unfortunately the medical student today is being taught on the lines of purely experimental pharmacology. It is little wonder that the initiates in medical practice are prescribing quite freely such highly dangerous drugs as phenobarbitone and using such antibiotics as penicillin in cases where other therapy would be safer and often much more successful.

Edinburgh, 9. JAMES BURNET.

FAMILIAL INCIDENCE OF LOW PSEUDOCHOLINESTERASE LEVEL

SIR,—The report by Dr. Lehmann and Miss Ryan (July 21) agrees with observations made here in Toronto.

Dr. D. R. Gunn found a few years ago some mental patients who were unusually susceptible to suxamethonium, and who had a very low esterase activity without any obvious cause. The existence of these cases stimulated an investigation into the nature of the esterase, along with a fairly extensive sampling of blood specimens from their family members, as well as from students, factory workers, and hospital patients.

The data suggest that there exist at least two types of human serum-cholinesterase. These types can be distinguished, for instance, by the use of the inhibitors neostigmine or cinchocaine, the local anæsthetic. It is advantageous to work with this latter compound because it is stable and inhibits instantaneously. With benzoylcholine as the substrate in 5×10^{-5} m. concentration, 10^{-5} m. cinchocaine inhibits the usual enzyme by 78% and the rare atypical form by less than 20%. Occasionally intermediate cases, showing an inhibition between 45 and 70%, are seen.

These data are compatible with the assumption of two allele genes for pseudocholinesterase giving rise to the two homozygous extremes and the heterozygous intermediates. The heterozygous group cannot be recognised with ordinary tests for esterase activity, while, with most of such tests, the atypical homozygotes are conspicuous because of their low activity. Hence, what appears to Lehmann and Ryan as a recessive gene seems to be an incompletely dominant gene, if one uses the inhibitor test. If these concepts are correct, the frequency of the atypical gene in a healthy population is $0{\cdot}0140 \pm 0{\cdot}0036$. That means the incidence of atypical homozygotes in a healthy population should be 1 in 5100, or rather between 1 in 3370 and 1 in 10,500.

To date we have considered this estimate with some reserve, because we know that there are 5 such cases among the 1379 mental patients (1 in 276) of the Ontario Hospital in New Toronto. However, Lehmann and

Ryan estimated the incidence as "well below 1 per 1000" by considering the frequency of abnormal reactions among surgical patients receiving suxamethonium. Since this count agrees with the gene frequency, the higher incidence among the patients of the mental institution may reflect a genetic relationship between type of pseudocholinesterase and incidence of mental illness. This possibility is being investigated.

Department of Pharmacology, University of Toronto, Canada. W. KALOW Associate Professor.

A MURDER CONVICTION QUASHED

SIR,—The case you reported (Sept. 1) of a U.S. serviceman who had a murder verdict quashed surely indicates the risks of relying solely on the findings of a necropsy. In view of this, would it not be wise for general practitioners who have previously attended a person who dies suddenly to be summoned to give evidence at the inquest? In my earlier days this was universal; today it is a great rarity.

London, N.4. CHARLES F. STOTT.

BURNS AND SCALDS

SIR,—On July 14 Prof. W. E. M. Wardill and his colleagues contributed to this correspondence a letter on their experience with the exposure treatment of burns.

Three months earlier, in April of this year, I saw with my own eyes granulations as they grow in Bagdad in the hot dry air under the care of Sister Jamila and Professor Wardill. They were as clear, dry, flat, and translucent as a newly varnished oil painting. There was neither crust nor pus. I saw no hint of contracture and my impression was that one might almost spit upon Iraqi granulations without infecting them! I was greatly impressed.

I find that in practice "treatment by exposure" is an elastic phrase. We plan to study the details of the Bagdad régime with a view to adapting and adopting it if possible. If my impressions and Professor Wardill's convictions are confirmed, as I sincerely hope they will be, we may look forward to a new chapter in the story of the treatment of burns.

Department of Surgery, University of Liverpool. CHARLES WELLS Professor of Surgery.

HEAVY FEET IN THE WARD

SIR,—We are grieved at the contention of Miss Hutchinson (Aug. 4) and Dr. MacWilliam (Aug. 18) that "a great many nurses do not know how to walk." Why single out nurses from the rest of the population? We agree that quiet-footed movements in hospital wards and elsewhere are in the interests of all concerned, but we suggest that it should not be impossible for even partial insulation of flooring to be achieved by the wide ranges of materials now available.

We cannot accept the statement that "it is very seldom anyone is taught the art" of walking. Firstly, the mother teaches her child to stand and to walk independently. Secondly, many schools teach physical culture in the form of gymnastics, games, or dancing.

Student nurses do, in fact, receive lectures and demonstrations on care of the feet during their first months in the training-school. These are normally given by a senior sister tutor and a physiotherapist. Also it is customary in most hospitals for all nurses on duty to wear rubber heels.

Where an individual fails to benefit from these opportunities—and that may be no fault of his own—the reasons may well be faulty posture, a lack of an inborn rhythmic sense or some power of coördination, such as the inability to hear oneself clattering around as others hear you, or some other hereditary defect common to everyone in greater or lesser degree.

Another practical consideration is the choice of suitable footwear, with emphasis on the proper fitting, especially during the years of growth. Nor can the influence of fashion on walking be ignored.

If then "The Child is the Father of the Man," what is the future of education in ambulation?

Kingston Hill, Surrey. ELIZABETH M. C. WILSON.
Petersham, Surrey. JEAN M. WARREN.

MIGRAINE TREATED WITH DEOXYCORTONE

SIR,—In a proportion of cases migraine might be explained by an upset of electrolyte and water balance leading to a rise in the intracellular-fluid content within the unyielding cranium. This explanation is supported by the polyuria that often follows an attack.[1]

In general practice I have now treated a small consecutive series of cases of severe migraine by injection of deoxycortone (desoxycorticosterone) acetate, with the idea of raising the level of circulating electrolytes and thereby reducing intracellular-fluid pressure.

CASE 1.—The first patient had a 40-year history of monthly attacks of migraine lasting 3 days with vomiting and photophobia. She felt "blown out" and gained weight before an attack, and as soon as polyuria started she knew she was going to improve. Two years ago an attempt was made to induce polyuria with mersalyl, intravenously, at the start of an attack; but this did not induce diuresis or change the usual form of attack. On the next occasion deoxycortone, 5 mg. in oily solution, was injected; and, though no dramatic improvement was noted, the migraine lasted only 2 days and there was no further attack for 6 months. After that, whenever she noticed oliguria and abdominal distension, which warn her of an attack, she had a prophylactic injection: this was necessary every 2 months. On this régime she had nothing worse than minor headaches. After two years she tried to do without the injections, and she had her usual severe 3-day migraine 3 months after the last injection.

Though the other nine cases (five females and four males) have not shown a history of water retention, I have treated them on similar lines, with good results in eight. The following examples may be of interest:

CASE 2.—A woman of 50 has had migraine with headache and vomiting about twice a week for 14 years. An injection of deoxycortone 5 mg. gave her 3 weeks' freedom, and I therefore inserted an implant of 25 mg. On this she had three headaches in 6 months, and after a further implant of 25 mg. she had two headaches at the end of a further 6 months. A 50 mg. implant was then inserted, and the headaches unexpectedly recurred, at intervals of 3 weeks. I found that scar tissue had formed round the implant, but in the 6 months since it was replaced she has had monthly headaches which seem to be precipitated by family crises.

CASE 3.—This patient developed rheumatoid arthritis 2 years ago and was free from migraine while on cortisone. The headaches returned when she was changed to corticotrophin but are relieved by the addition of 5 mg. deoxycortone every two months.

CASE 4.—This patient said that she had been free of headaches when pregnant. She has been completely relieved by deoxycortone.

Deoxycortone does not prevent, or relieve, an attack unless given at least 2 days (preferably a week) before an attack is due.

These were long-established cases of migraine (the mean duration of their symptoms was over 20 years), and they had been treated by many different methods, from desensitisation to psychotherapy and from vitamins to vasodilators. Hence I think that the good results I have obtained with deoxycortone cannot be due to suggestion. I hope that colleagues with more cases of migraine under their care may be inclined to undertake a controlled trial.

Jersey. H. L. DURELL.

1. Edwards, C. H. *Postgrad. med. J.* 1954, **30**, 228.

MIGRAINE TREATED WITH CHORIONIC GONADOTROPHIN

SIR,—In the fourteen years since I proposed the use of chorionic gonadotrophin for treating migraine,[1] modifications of the method have been made [2] and its value has been confirmed by others.[3 4] The following case is of interest, not particularly because of the successful outcome, which is common, but because the patient developed hirsuties.

A district nurse began to have periodic headaches in 1944, at the age of 23. In 1948 these became worse and in the next six years she was seen by a number of neurologists and had various forms of treatment without benefit. When I saw her first in 1954, she was still at work but was taking *every day* sixteen codeine tablets (gr. $^1/_2$) as well as phenobarbitone (gr. 2) and 'Dromoran' half a tablet (0·75 mg.) night and morning.

Regarding her migraine as of combined allergic and endocrine type, I prescribed a course of chorionic gonadotrophin (ultimately 500 units twice weekly), also attempting desensitisation with neostigmine.[5] Improvement was noted after the first month and continued until February, 1955, three months after the course finished. When she was seen in March, 1955, there had been a slight return of the headaches; endocrine therapy was reinstituted, and after two months she was again headache-free.

In April, 1956, she noted an increase in hair growth: there was fine down on the cheek, with additional hair under the arms and in the pubic area, and the hair on the thighs had become longer and thicker. She ceased taking the gonadotrophin, and after six weeks the additional hair growth had receded; but the headaches had returned. She therefore resumed therapy and they were again relieved in two weeks.

In July a twenty-four-hour sample of urine contained: 17-ketosteroids, 25·7 mg.; 17-hydroxycorticoids, 20·2 mg.; pregnanetriol, 2·9 mg.; pregnanediol, 9·6 mg.; œstrone, 27·3 µg.; œstradiol, 2·1 µg.; œstriol, 17·2 µg.

The patient has now been advised to reduce the dosage of gonadotrophin to 100 units weekly.

It is difficult to explain why this patient reacted as she did, for many have had far longer courses of chorionic gonadotrophin without any untoward results. She told me, however, that in order to relieve her otherwise intolerable headaches she would continue with the endocrine therapy, even if it meant the continued growth of hair.

Chorionic gonadotrophin is said to act via the pituitary and not directly on the gonads.[6]

Migraine Clinic,
Putney Health Centre,
London, S.W.15. NEVIL LEYTON.

UNIVERSITY COLLEGE, LONDON

Sir Ifor Evans, provost of University College, London, writes:

I should be grateful if you would grant me a little space in your columns to try and make contact with old students of University College London, of whom we calculate there must be some 30,000 either in this country or overseas. Unfortunately, we have got records of the careers and up-to-date addresses of only a very small proportion of this number. The college authorities are anxious to get in touch with old students, to invite them when possible to appropriate college functions, and on occasion to seek their advice. It is only when some honour, public appearance, or other matter is recorded in the press that the college can add to its records of the individual concerned.

The college authorities hope that old students will write, even just a postcard, to the Secretary of University College London, Gower Street, London, W.C.1, giving their addresses, dates at college, and subjects studied, and will keep the secretary informed of changes of address.

1. Leyton, N. *Lancet*, 1942, i, 448.
2. Leyton, N. Migraine and Periodic Headache. London, 1952.
3. Ross, F. *Nova Scotia med. Bull.* December, 1950.
4. Sweetnam, M. T. *Practitioner*, April, 1956, p. 431.
5. Pelner, L., Aibel, M. E. *J. Lab. clin. Med.* 1942, **27**, 1546.
6. Fraenkel-Conrat, H. L., Simpson, M. E., Evans, H. M. *J. biol. Chem.* 1939, **130**, 243.

Public Health

A Search for Diabetes

THE medical officer of health for Salford, Dr. J. L. Burn, has lately described [1] the results of a search for diabetes carried out concurrently with routine mass-miniature radiography (M.M.R.). Excluding children under 15, expectant mothers, and National Service entrants, between 4000 and 5000 candidates for M.M.R. were invited to submit a urine specimen. 2165 (47·3%) people did so, and rapid sorting with 'Clinitest' tablets produced 150 samples positive for sugar. Those were then tested by the standard clinitest technique, reducing the positives to 31. At that stage, the 31 patients were asked to furnish a second specimen of urine for more detailed examination. The final outcome was that 6 previously undetected diabetics (a rate of 2·6 per 1000) and 10 cases of renal glycosuria were identified and referred to their own doctors or to diabetic clinics.

The Salford survey may make us change our ideas about M.M.R. units. Given a local community conditioned to the idea of periodical routine X-ray examinations of the chest, there may be scope for offering a wider range of survey or diagnostic services to voluntary attenders. As in the diabetes survey, some entirely different field might be explored without greatly hampering the primary function of the unit. It may be that the M.M.R. unit will be absorbed into a larger service, mobile wherever techniques permit, but becoming more static if anything like health centres or diagnostic centres come into wide use.

In the United States some of the large insurance companies have long been trying to persuade the public of the value of regular diagnostic tests, with the result that it is not uncommon for a perfectly healthy businessman to call on his doctor and ask for a full "check-up." But few general practitioners in the National Health Service would care to undertake many such examinations. Periodical medical boards on every citizen may be a not unreasonable obligation of the social and sickness insurance schemes of the welfare state. The day of compulsory boards, however, is a long way off and many would oppose any steps to bring it nearer; but there can be few objections to volunteers coming forward for examination as they did at Salford.

Hospital Provision for Smallpox

A Ministry of Health memorandum [2] suggests ways of reviewing arrangements for the hospital accommodation of patients with smallpox. Several of the existing effective smallpox hospitals no longer comply with the conditions (prescribed as long ago as 1924) about how far away the hospital should be from other buildings and how many people may live near to it. A number of hospitals once available have, in fact, been so closely enveloped by houses that they are no longer considered safe for smallpox.

In each region one or two small hospitals are held empty in readiness for smallpox cases; and these hospitals are supported by a further line of infectious-diseases or other hospitals which can be evacuated when necessary. The cover provided is so widely dispersed that situations will almost certainly arise, the memorandum says, when for clinical, meteorological, or geographical reasons it would be unwise to transport a patient to a remote first-line hospital. It will then be necessary to admit the patient to an infectious-diseases hospital. In that event, if smallpox is retained in such a hospital, either the hospital should be cleared of other patients or a separate part of it must become a self-contained unit.

In selecting this auxiliary accommodation, it is essential, the Ministry emphasises, that the location of the hospital chosen and the lay-out of its buildings should allow segregation of patients and staff from the general public. The 1924 recommendations attempted to segregate by remoteness, which minimised the risk of contact. Few hospitals now retain that remoteness.

1. *Med. Offr*, 1956, **96**, 5.
2. H.M.(56)79.

but the same end can be achieved in suitable buildings, provided the staff is vaccinated, disciplined, and well supervised.

As for first-line hospitals, the Ministry's view is that the small ad-hoc hospital kept on a care-and-maintenance basis and immediately available to receive patients is the safest insurance. A nucleus of such accommodation coming as near as possible to the 1924 standards should be maintained in each region.

Finally, the memorandum declares, it cannot be emphasised too strongly that anyone connected in any way with a hospital in which smallpox is being treated must be revaccinated, preferably before contact. The records of all outbreaks since the war have underlined the importance of vaccination for staff, especially those who may unwittingly be in contact with smallpox not yet diagnosed.

Poliomyelitis

Uncorrected notifications of poliomyelitis in England and Wales during the week ended Sept. 1 were as follows: paralytic 53 (63), non-paralytic 71 (114); total 124 (177). This is a decrease of 53 compared with the previous week, the figures for which are in parentheses.

Obituary

HENRY PERCY PICKERILL

C.B.E., M.D., M.Ch., M.D.S. Birm., F.R.A.C.S.

Mr. H. P. Pickerill, consulting plastic surgeon to the Wellington Hospital, New Zealand, died on Aug. 10 at the age of 77. In the first world war he became known for his work on maxillo-facial injuries, but many doctors in this country and in this decade will remember him best for the enterprise of his old age, when he successfully eliminated cross-infection from a children's hospital by bringing the mother to the bedside.

Pickerill was born and educated in Hereford, and he was articled to a dental surgeon there till, in 1900, he went to Birmingham University to continue his studies. After taking the L.D.S. in 1903 and the B.D.S. Birm. in 1904 he became a demonstrator at the Birmingham Dental Hospital. While holding this post he took the M.B. Birm. in 1905. The following year he was appointed assistant surgeon to the hospital and a lecturer on dental histology and pathology in the university. In 1910 he was awarded the Cartwright prize and medal of the Royal College of Surgeons of England for his essay on the prevention of dental caries. The following year he proceeded to the degrees of M.D. and M.D.S.

Soon afterwards he went to New Zealand to take up the post of professor and dean of the dental school of Otago. In the next few years he made his first contribution to the founding of dental education in New Zealand. He was an excellent teacher both of theory and practice, and his fresh inquiring mind compared with interest the vast amount of caries among the generally well-nourished New Zealanders with the much lower incidence among the Maori children. He wrote as well as he taught, and his book on the buccal cavity, *Stomatology* (1915), was widely used by medical as well as dental students.

Soon after war broke out in 1914 he returned to England with the 1st New Zealand Expeditionary Force. His work among the casualties stimulated his interest in maxillo-facial surgery and, with the rank of lieut.-colonel in the New Zealand Medical Corps, he was appointed officer in command of the New Zealand section at Queen Mary's hospital for facial injuries at Sidcup. He was appointed O.B.E. for these services in 1919. After his return to New Zealand he continued this work as surgeon in charge of the facial and jaw department at the Dunedin Hospital, and in 1923 he was promoted C.B.E.

In 1924 he resigned from his post at the dental school in Dunedin to give all his time to plastic surgery, especially of the lips and palate. In 1927 he moved to Sydney, where he established himself in consultant practice and joined the staff of the Royal North Shore Hospital. In 1930 he was elected F.R.A.C.S. In 1935 he returned to New Zealand and settled in Wellington. Here again he quickly acquired a consultant practice and hospital appointments. With his second wife, Dr. Cecily Pickerill, he set up the Bassam Hospital, and during the past ten years in articles and letters in our columns they have described how they have controlled cross-infection by admitting each child with its mother and allotting a small private room to each pair. For many years Mr. Pickerill had been interested in the problems of metastases, but the second world war interrupted this work and weakened his health. Later, in his own words, "I decided to drop my metastatic work in favour of attacking the problem of making surgery safe for infants and infants safe for surgery." The record of the Bassam Hospital shows how successfully he solved his chosen problem.

A colleague writes:

Pickerill was a man of great and original intelligence and insight whose medical interests covered a much wider range than plastic surgery and odontology. He was always stimulating to talk to, provocative, and almost quarrelsome at times. In his youth he was a fly fisherman and mountain-climber, a keen gardener, and fond of music until deafness overtook him. He was an Anglican lay-reader in his younger days, and felt keenly on social problems such as judicial hanging. Pick will be remembered affectionately and with admiration by many medical and dental colleagues throughout the Commonwealth.

Mr. Pickerill was twice married. His second wife, Dr. Cecily Pickerill, survives him with their daughter. He also leaves a daughter and three sons by his first marriage. One son, who is a dental surgeon, lately read the address which his father had prepared but was unable to deliver at the 50th anniversary of the founding of the Otago University Dental School.

Births, Marriages, and Deaths

BIRTHS

FRYER.—On Sept. 3, at Aldershot, to June (née Bradley), wife of Squadron-Leader D. I. Fryer—a son (Martin John).

MARRIAGES

BEGG—GOLDSPINK.—On Sept. 5, at St. Ninian's Presbyterian Church, Golders Green, Douglas Andrew Begg, M.B., to Christine Margaret Goldspink, S.R.N., S.C.M.

Appointments

HALE, B. T., M.B. Brist., D.M.R.T.: asst. radiotherapist, United Bristol Hospitals.

HOPPER, J. M. H., M.B. Durh., D.OBST.: school M.O., co. Durham.

MCDONALD, A. B., M.B. Glasg., D.M.R.E.: whole-time consultant radiologist, Durham and North West Durham H.M.C. areas.

MACLEAN, NEIL, M.B. Edin., M.R.C.P.E., D.P.H.: whole-time asst. pathologist, Edinburgh Northern group of hospitals, based on the Western General Hospital.

PICK, D. P., M.B. Edin.: school M.O., co. Durham.

SUMPTION, J. C., M.B. Lond., F.F.A. R.C.S., D.A.: consultant anæsthetist, Pontypridd and Rhondda H.M.C. area.

WALES, W. T. H., M.R.C.S., D.P.M.: medical superintendent (consultant psychiatrist), Pen-y-Val Hospital, Abergavenny.

WELSH, WALTER, L.R.C.P.E.: school M.O., co. Durham.

East Anglian Regional Hospital Board:

BROWNE, R. A., M.B. Aberd., D.A.: anæsthetic registrar, West Suffolk General Hospital.

HICKS, MARGARET J., M.B., B.SC., Wales: pædiatric registrar, Ipswich and East Suffolk Hospital.

PRINGLE, H. M., M.B. Sydney: surgical registrar, West Suffolk General Hospital.

SIMS, S. R., M.B. Lond.: asst. chest physician, Peterborough and Huntingdon chest clinic areas.

STANDING, D. G., M.B. Cape Town: registrar in obstetrics and gynæcology, Peterborough group of hospitals.

Notes and News

POST-SUBSIDY FLOUR

THE National Association of British and Irish Millers has announced that after Sept. 29, when the bread subsidy ends, the following new types of flour will be available to bakers:

A new white-bread flour, similar in quality to pre-war, and enriched with the prescribed nutrients. This will be the basic grade and should be sold at the same price as "National" flour.

A superfine white-bread flour, also enriched and selling at a premium above the basic grade.

A softer type of white-bread flour selling at a discount below the basic grade. This is a flour which some bakers may require for special purposes and for mixing in with stronger bread-flours.

A high extraction "off-white" flour, deriving its nutrients solely from the milling process.

The existing brown, wheatmeal and wholemeal specialty types of flour sold to bakers will be unaffected.

The association states that the four types of flour will "achieve the nutritional level" of vitamin B_1, nicotinamide, iron, and calcium laid down in the new Flour (Composition) Regulations, 1956, under the Food and Drugs Act.[1]

T.U.C. AND SMOKING

AT the Trades Union Congress in Brighton last week a motion from the Medical Practitioners' Union was proposed by Dr. Arnold Elliott, calling on the Government "to take all reasonable steps to discourage young people from smoking" in view of the accumulation of evidence that smoking is one of the principal causes of the five-fold increase in the number of deaths from lung cancer during the past 15 years. The motion was supported by the Association of Scientific Workers, but the congress voted in favour of an amendment, proposed by the Tobacco Workers' Union, which noted the increase in the number of deaths, but ended as follows:

"and recognizing that eminent medical authorities have so far failed to agree about its possible causes, calls on the Government to give all possible assistance in the furtherance of research into this dread disease."

University of London

On Thursday, Nov. 1, at 5 P.M., at the Royal Society of Medicine, 1, Wimpole Street, W.1, Prof. Georges Portmann, of the University of Bordeaux, will deliver the Semon lecture. Professor Portmann is to speak on the physiology of phonation.

University of Birmingham

On Monday, Oct. 1, at 3 P.M., at Queen Elizabeth Hospital, Dr. Walter Bauer, Jackson professor of clinical medicine in the Harvard Medical School, will deliver the inaugural address of the session.

Royal College of Physicians of London

On St. Luke's Day, Thursday, Oct. 18, at 3 P.M., at the college, Pall Mall East, S.W.1, Dr. J. Crighton Bramwell will deliver the Harveian Oration. His subject will be Practice, Teaching, and Research.

Royal College of Physicians of Edinburgh

On Thursday, Oct. 11, Prof. W. J. Tulloch will speak on medicine as an aspect of general biology. On Friday, Nov. 9, Dr. W. Ferguson Anderson will deliver the John Matheson lecture, when his subject will be the care of the elderly sick in general practice. On Tuesday, Nov. 27, the Sydney Watson Smith lecture will be given by Dr. John McMichael, who will speak on valvular incompetence and heart-failure. All the lectures begin at 5 P.M.

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the faculty on Sept. 3, with Prof. Stanley Graham, the president, in the chair, the following were admitted fellows of faculty:

Gerard Church, I. W. W. Fingland, Damodaram Harirajan, Kailash Nath Kanwar, J. B. McGuinness, Penmetcha Venkata Narasimha Raju, Niranjan Lall Sharma.

Welsh National School of Medicine

This school is celebrating on Oct. 12 and 13 the 25th anniversary of the granting of its charter. A dinner is to be held on the 12th, and invitations have been sent to all old students who can be traced. Anyone who has not yet received an invitation should write to the secretary of the school, 34, Newport Road, Cardiff.

1. See *Lancet*, Aug. 11, 1956, p. 301.

Royal Free School of Medicine

Sir Francis Walshe, F.R.S., will deliver the inaugural address to this school on Friday, Oct. 5, at 3 P.M. at the Senate House, London, W.C.1.

Westminster Medical School

On Monday, Oct. 8, at 3 P.M., Viscount Chandos will deliver the inaugural address to this school at Church House, Great Smith Street, S.W.1.

Royal Society of Tropical Medicine and Hygiene

The opening meeting of the session will be held at 26, Portland Place, London, W.1, on Wednesday, Oct. 10, at 7.30 P.M., when Dr. H. A. Reid will read a paper on Sea-snake Research.

King's College Hospital Medical School

On Friday, Sept. 28, Lord Justice Denning will give the inaugural address at this school, Denmark Hill, London, S.E.5, at 3 P.M.

Society of Apothecaries of London

Liverymen are summoned to meet at Guildhall on Saturday, Sept. 29 (not Sept. 28 as announced in our issue of Sept. 1), at 10.30 A.M., to elect a lord mayor of the city.

Biochemical Society

A meeting of this society will be held at the National Institute for Medical Research, Mill Hill, London, N.W.7, on Friday, Oct. 12, at 2 P.M.

British Postgraduate Medical Federation

Sir John Cockcroft, D.SC., F.R.S., will give the inaugural lecture of the 1956–57 series on the Scientific Basis of Medicine at 5.30 P.M. on Thursday, Oct. 11, at the Senate House, University of London, Malet Street, W.C.1. He is to speak on the Biological Significance of Atomic Energy.

London County Medical Society

At a meeting of this society to be held at County Hall, Westminster Bridge, S.E.1, on Thursday, Oct. 4, at 5.30 P.M., Sir Clement Price Thomas will speak on Carcinoma of the Lung. Members of the Association of Industrial Medical Officers, the Middlesex County Medical Society, and all London divisions of the British Medical Association are invited.

Institute of Diseases of the Chest, London

Clinical demonstrations will be given by Dr. E. H. Hudson at the institute (in the grounds of the Brompton Hospital, Fulham Road, S.W.3) on Fridays from Oct. 5 to Dec. 14. Open lectures by Mr. N. R. Barrett, Dr. N. Lloyd Rusby, Dr. N. S. Plummer, Mr. J. R. Belcher, Mr. W. P. Cleland, Dr. I. S. Longmuir, Dr. N. C. Oswald, Mr. T. Holmes Sellors, Dr. W. E. Lloyd, and Dr. A. I. G. McLaughlin will be given on Wednesdays, from Oct. 3 to Dec. 5. All the meetings will be held at 5 P.M. and will be open to doctors without fee.

International Society for the Study of Bioclimatology

The purpose of this society, which was founded on Jan 1, 1956, is to unite into one international group all those interested in the influence of climate on air, water, soil, plants, animals, and man, in the hope of discovering the factor, or factors, responsible for this influence. The first meeting was held from Aug. 29 to 31 at UNESCO House in Paris, when Dr. F. Sargent (U.S.A.) was elected president. Eighteen different countries were represented. It is proposed to hold the next meeting in the autumn of 1957 in Vienna. Further information may be had from Dr. S. W. Tromp, Hofbrouckerlaan 54, Oegstgeest (Leyden), Holland.

CORRIGENDUM: *Antibiotics in Preservation of Fish.*—Our note of June 23 (p. 1009) implied that salt was widely used for checking bacterial spoilage of fish while stored on the fishing vessel. In fact, it is seldom used and ice is the accepted method of preserving at sea. The chlortetracycline was incorporated in ice, not in salt.

Sir Robert Macintosh and Prof. Ian Aird are to visit Poland in October to lecture to specialist audiences. The visit has been arranged by the British Council at the request of the Polish ministry of health.

Bayer Products Ltd. have published a pamphlet showing the tablet markings adopted by the company. The pamphlet shows, for each different tablet, the markings on the upper face and the reverse face, the diameter, the shape, and the colour. Copies may be had from the company, Neville House, Eden Street, Kingston-on-Thames, Surrey.

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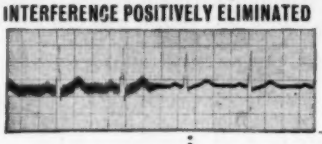

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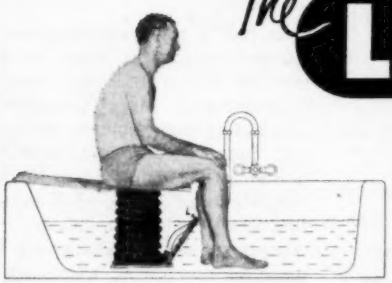

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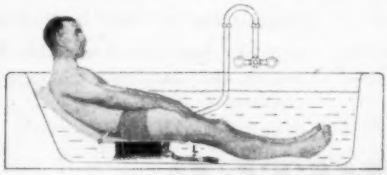

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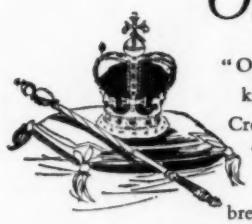

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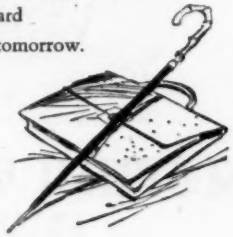

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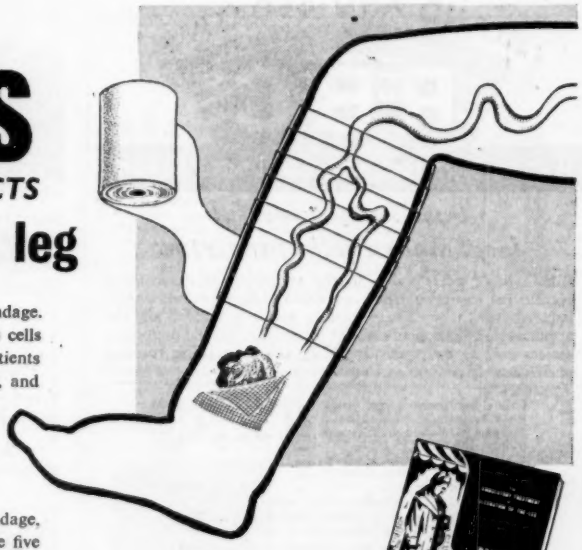

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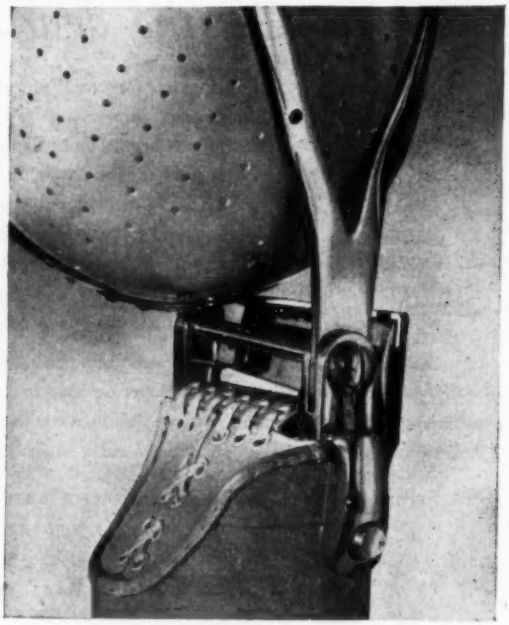

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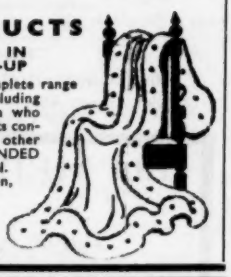

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Further information from the Secretary, Tuberculosis Educational Institute, Tavistock House North, Tavistock-square, London, W.C.1.

DENTAL AND MEDICAL SOCIETY FOR THE STUDY OF HYPNOSIS

The above society will hold a STUDY GROUP ON THE THEORY AND PRACTICE OF HYPNOSIS beginning on WEDNESDAY, 3RD OCTOBER, 1956. 2-hour lecture-demonstrations will begin at 7.15 P.M.

An INTENSIVE WEEKEND COURSE will be held on 24TH and 25TH NOVEMBER for members who live too far away from London to attend the full course.

A fee is charged for these Study Groups.

The Society is prepared to send a team of lecturers and subjects to any locality in Great Britain to give an intensive weekend course provided that sufficient Medical and Dental practitioners are willing to attend.

Further details may be obtained from the Secretary, Mr. DAWSON WATTS, 22, Gordon-road, Ealing, W.5.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, London, W.C.2. Required, in the Pathological Department, Full-time RESEARCH PATHOLOGIST to combine working in the Department with performing post-mortem examinations and gaining experience in forensic pathology. Preliminary training in general pathology an advantage. Appointment initially for 1 year and subject to extension. Salary according to age, qualifications and experience, in range £900–£100–£1300.

Applications, with the names of 2 referees, to be addressed to the Secretary, Royal College of Surgeons. Closing date 1st October, 1956.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. Applications are invited for the appointment of a RESEARCH FELLOW IN SURGICAL PATHOLOGY to work in the Department of Morbid Anatomy on problems of urological surgery and pathology, viz., hydronephrosis and hydro-ureter. Previous experience in morbid anatomy essential. The appointment will be for 1 year in the first instance, renewable for 1 or 2 further years, within the salary range £1100–£1400 p.a.

Further particulars and forms of application, which should be returned by 24th September, 1956, may be obtained from the House Governor.

THE WELSH NATIONAL SCHOOL OF MEDICINE. (UNIVERSITY OF WALES.) Applications are invited for the appointment of ASSISTANT CLINICAL PATHOLOGIST in the Department of Pathology and Bacteriology. Previous experience in pathology is not essential. The appointment is a full-time one for a period of 2 years within the salary scale £750–£100–£1050 p.a., with participation in family allowance and superannuation schemes. The point of entry on the scale will depend on qualifications and experience.

Applications should be sent by 20th October, 1956, to the undersigned, from whom further particulars of the appointment may be obtained.

34, Newport-road, Cardiff. F. DODSWORTH, Secretary.

UNIVERSITY OF LONDON. The Senate invite applications for the JOHN ASTOR CHAIR OF PHYSIOLOGY tenable at Middlesex Hospital Medical School (salary within the range £2250–£2850 a year).

Applications (10 copies) must be received not later than 18th October, 1956, by the Academic Registrar, University of London, Senate House, W.C.1, from whom further particulars may be obtained.

UNIVERSITY OF LONDON. The Senate invite applications for the READERSHIP IN PATHOLOGY tenable at Westminster Medical School (salary within the range £1900–£2400 a year).

Applications (10 copies) must be received not later than 16th October, 1956, by the Academic Registrar, University of London, Senate House, W.C.1, from whom further particulars may be obtained.

UNIVERSITY OF BRISTOL. Applications are invited for the post of ASSISTANT LECTURER (grade III) or DEMONSTRATOR IN PHARMACOLOGY. Medical qualifications desirable but not essential. Initial salary £550–£700 p.a. according to qualifications and experience, together with superannuation and children's allowances. The successful candidate will be expected to devote much of his time to research. The post would be suitable for a candidate who wishes to read for a higher degree.

Further particulars may be obtained from the Registrar of the University to whom applications, with the names of 3 referees, should be sent not later than 8th October.

UNIVERSITY OF BRISTOL. Applications are invited from registered medical practitioners for the new post of LECTURER IN FORENSIC PATHOLOGY in the University Department of Pathology. The duties include the conduct of autopsies, with special responsibility for those of medico-legal importance. The terms and conditions of the appointment will be those appropriate to a Clinical Lecturer and the commencing salary will be in the range of £1750–£100–£2400, together with superannuation and children's allowances. All fees received are to be paid to the University.

Applications, with the names of 3 referees, should be made to the undersigned, from whom further particulars may be obtained, not later than 1st October, 1956.

H. C. BUTTERFIELD, Registrar and Secretary.

UNIVERSITY OF EDINBURGH. Medical Physics Unit. Applications are invited for the post of DIRECTOR of the Medical Physics Unit with status of Senior Lecturer. This Unit is being established jointly by the University and the South-Eastern Regional Hospital Board, Scotland. Salary scale £1750–£100–£2250 p.a., with superannuation benefit and, where applicable, family allowance.

Further particulars may be obtained from the Secretary to the University, Old College, South Bridge, Edinburgh, with whom applications, giving the names of 3 referees, should be lodged by 1st November, 1956.

UNIVERSITY OF GLASGOW. Applications are invited for a LECTURESHIP in the Department of Medicine at the Western Infirmary. Salary according to placement on University scale for clinical teachers. The final maximum is £1750 p.a. F.S.S.U. and family allowance benefits.

Applications (12 copies) should be lodged, not later than 3rd October, 1956, with the undersigned, from whom further particulars may be obtained.

ROBT. T. HUTCHESON, Secretary of University Court.

UNIVERSITY OF OXFORD. Department of Pathology, RADCLIFFE INFIRMARY. Applications are invited for the post of SENIOR RESEARCH OFFICER IN NEUROPATHOLOGY, for a period of 5 years in the first instance. Salary scale £1000–£50–£1700; F.S.S.U. and family allowance. The successful candidate will be expected to take up duties in the early part of Michaelmas Term, 1956. Preference would ordinarily be given to candidates with experience in neuropathology, but favourable consideration would be given to candidates experienced in general morphological pathology who would wish to specialise in neuropathology. In addition to some teaching duties and facilities for research, the duties include the investigation of the neurosurgical and neurological specimens of the United Oxford Hospitals.

Applications, with the names of 2 referees, should be sent by 6th October to Dr. A. H. T. ROBB-SMITH, Department of Pathology, Radcliffe Infirmary, Oxford, from whom further particulars may be obtained.

UNIVERSITY OF OXFORD. The University proposes to appoint a UNIVERSITY DEMONSTRATOR IN BIOCHEMISTRY from 1st January, 1957, or as soon as possible thereafter, at a stipend in the scale £750–£50 (at age 29)–£1100–£100–£1200–£50–£1450. The stipend is in the scale £1000–£50–£1700 if the demonstrator is medically qualified. Membership of F.S.S.U. necessary. Allowance of £50 p.a. for each dependent child.

Applications (4 copies), stating age, qualifications, and experience, and giving the names of 2 referees, to Prof. H. A. KREBS, Department of Biochemistry, South Parks-road, Oxford, from whom further particulars may be obtained, not later than 31st October, 1956.

FOURAH BAY COLLEGE, Sierra Leone. (University OF DURHAM.) Applications are invited for appointment as COLLEGE MEDICAL OFFICER from fully qualified and experienced medical practitioners, preferably with experience in the tropics. The post is tenable on contract terms—salary scale £1098–£1350 E.B. £1452–£1898; point of entry determined by qualifications and experience. Other emoluments include children's allowances and gratuity.

Further information may be obtained from the Secretary, Advisory Committee on Colonial Colleges, 1, Woburn-square, London, W.C.1. Closing date for applications—28th September, 1956.

Hospital Services: Senior Appointments

SOUTH WEST METROPOLITAN REGIONAL HOS-PITAL BOARD requires Whole-time SENIOR CASUALTY OFFICER (salary scale £1575–£50–£2025 p.a.) at St. James' Hospital, Balham, S.W.12, to work with the Trauma and Orthopædic Unit and be in charge of a large Casualty Department. (2 Casualty Officers, 20,000 new cases annually.) Candidates must possess F.R.C.S. The appointment will be for a period not exceeding 4 years.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 6th October, 1956. Applicants may visit Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOS-PITAL BOARD requires Whole-time CONSULTANT CLINICAL PATHOLOGIST for the Fulham and Kensington Group Laboratory at St. Mary Abbots Hospital, W.8. Candidates should have special interest and experience in chemical pathology.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 13th October, 1956. Applicants may visit Laboratory by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOS-PITAL BOARD requires Part-time CONSULTANT PATHOLOGIST (7 half-days per week) for the St. Helier Group of hospitals. Duties mainly at Nelson Hospital, S.W.20, and Wimbledon Hospital, S.W.20.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 13th October, 1956. Applicants may visit hospitals by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOS-PITAL BOARD requires Part-time CONSULTANT PHYSICIAN (2 half-days per week) for the Fulham and Kensington Group of hospitals. Duties at St. Mary Abbots Hospital, W.8. 1 inpatient and 1 outpatient session weekly.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 13th October, 1956. Applicants may visit Hospital by local arrangement.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.

(1) ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade), Child Guidance Training Centre, 6, Osnaburgh-street, N.W.1, for 4 half-days a week. Applicants should have undergone training in child psychiatry and had some subsequent experience. Centre may be visited by direct appointment.

Applications before 15th October, 1956.

(2) CONSULTANT OTOLOGIST (initially 1 session per week) to Heston School for the Deaf, Vicarage Farm-road, Heston, and Director of the Audiology Unit to be established. The successful candidate will be responsible for the development of this Unit which will undertake the diagnosis and auditory training of the deaf and partially deaf pre-school child and the care of the older partially deaf child in ordinary schools. Candidates should have considerable experience of this type of work. Unit may be visited by arrangement with the Area Medical Officer, 92, Bath-road, Hounslow.

Applications before 17th October, 1956.

(3) CONSULTANT PHYSICIAN (whole-time), St. Pancras Chest Clinic, 26, Margaret-street, W.1. Good general medical experience and special experience in chest diseases essential. The Physician appointed will have charge of 47 Beds at Whittington Hospital, Highgate Wing. Post vacant 18th March, 1957. Clinic may be visited by direct appointment.

Applications before 22nd October, 1956.

(4) ASSISTANT PHYSICIAN in Physical Medicine (2 half-days a week), Senior Hospital Medical Officer grade, King Edward Memorial Hospital, Ealing (151 Beds). Hospital may be visited by direct appointment.

Applications before 26th October, 1956.

Application forms obtainable from, and returnable to, Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1.

BARROW AND FURNESS HOSPITAL MANAGEMENT COMMITTEE. Locum Tenens ANÆSTHETIST required for period of at least 6 months, commencing as soon as possible, in the Barrow and Furness Group of hospitals. Remuneration 31½ guineas per week, or 45 guineas per week if medical practitioner appointed has a personal grading of Consultant.

Applications to Group Secretary, 105, Abbey-road, Barrow-in-Furness, immediately.

LIVERPOOL REGIONAL HOSPITAL BOARD. Applications are invited for the post of Part-time CONSULTANT PÆDIATRIC SURGEON on maximum sessions with duties mainly at Alder Hey Children's Hospital and some duties at Birkenhead Children's Hospital. Applicants must possess the F.R.C.S. and have had wide experience in children's surgery. Special experience in surgery of newborn infants would be an advantage.

Forms of application from, and to be returned to, Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James-street, Liverpool, 2, to be received not later than 6th October, 1956.

VINCENT COLLINGE, Secretary to the Board.

LIVERPOOL REGIONAL HOSPITAL BOARD. St. Helens AND DISTRICT AREA. Applications are invited for the post of Whole-time ASSISTANT CHEST PHYSICIAN (Senior Hospital Medical Officer). Duties, which will be under the supervision of the Consultant Chest Physician, will include work at the chest clinics and hospitals in the area providing beds for the treatment of tuberculosis. Candidates should hold a higher degree or diploma, and should have had extensive experience in the diagnosis and treatment of diseases of the chest including tuberculosis.

Forms of application from, and to be returned to, Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James-street, Liverpool, 2, to be received not later than 6th October, 1956.

VINCENT COLLINGE, Secretary to the Board.

LIVERPOOL REGIONAL HOSPITAL BOARD. Applications are invited for the post of Whole-time ASSISTANT PATHOLOGIST (Senior Hospital Medical Officer) for duties in the Warrington Group of hospitals and Winwick Hospital. The main duties will be centred on the Warrington Infirmary and Warrington General Hospital.

Forms of application from, and to be returned to, Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James-street, Liverpool, 2, to be received not later than 6th October, 1956.

VINCENT COLLINGE, Secretary to the Board.

MANCHESTER REGIONAL HOSPITAL BOARD.

(*a*) Whole-time CONSULTANT GROUP PATHOLOGIST, North and Mid-Cheshire Group of hospitals, mainly at Altrincham General Hospital, near Manchester. Existing laboratory being improved and extended. Good training and experience in all branches of hospital pathology essential. 3rd October, 1956.

(*b*) Part-time (8 half-days weekly) CONSULTANT E.N.T. SURGEON to North and Mid-Cheshire Hospitals (about 4 sessions, mainly at Altrincham General Hospital E.N.T. Department) and Manchester Ear and Wythenshawe Hospitals (2 sessions each). Wide experience and higher qualifications essential, appointee to live in Altrincham area. 5th October, 1956.

Application forms from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, to be returned by dates stated.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. WEST MIDDLESEX HOSPITAL. MASS MINIATURE CHEST X-RAY UNIT. Locum Tenens SENIOR HOSPITAL MEDICAL OFFICER for 2 sessions a week to undertake reading of miniature films. Previous experience in this work or in general X-ray diagnosis advantageous. Post will last for 1 year or longer.

Application forms obtainable from, and returnable to, Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 26th September, 1956.

NORTH GLOUCESTER CLINICAL AREA. SOUTH-WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of Locum Tenens CONSULTANT in Anæsthetics to undertake whole-time duties mainly at the Gloucestershire Royal Hospital, Gloucester.

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, should be sent immediately, to the Secretary of the Regional Hospital Board, 27, Tyndall's Park-road, Bristol, 8.

NEWCASTLE REGIONAL HOSPITAL BOARD. Durham HOSPITAL MANAGEMENT COMMITTEE. Locum RADIOLOGIST (whole-time) for 5–6 months. Salary according to grade.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6.

OXFORD REGIONAL HOSPITAL BOARD: SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. CONSULTANT PÆDIATRICIAN (part-time—9 sessions), in the Wiltshire/Gloucestershire area. 6 of the sessions will be with the Swindon/Cirencester area department and 3 with the Salisbury Group of hospitals. Wide experience and a higher medical qualification are essential. The successful candidate will be required to live in the Marlborough area.

Applications (12 copies), stating name, age, qualifications and experience, together with the names of 3 referees, should reach the Secretary, Oxford Regional Hospital Board, 43, Banbury-road, Oxford, not later than 6th October, 1956.

OXFORD REGIONAL HOSPITAL BOARD. Consultant PSYCHIATRIST (Deputy Physician-Superintendent) to the Pewsey Mental Deficiency Hospital and Ancillary premises (960 Beds). Whole-time or maximum part-time. Residential accommodation available. Candidates must hold the D.P.M. and be familiar with the statutory responsibilities prescribed by the M.D. acts and regulations. The hospitals may be visited by arrangement with the Secretary, Pewsey Hospital, Pewsey, Wilts.

Applications (12 copies), stating age, qualifications, experience and the names of 3 referees, to the Secretary, Oxford Regional Hospital Board, 43, Banbury-road, Oxford, by 6th October, 1956.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of CONSULTANT PHYSICIAN at the Western Infirmary, Glasgow. The appointment will be part-time, remunerated on the basis of 8 notional half-days per week. This appointment is subject to the National Health Service (Scotland) superannuation regulations.

Applications (16 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, not later than 30 days after the publication of this advertisement.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for 2 appointments as CONSULTANT in Radiodiagnosis at the Royal Infirmary of Edinburgh. The appointments will be whole or maximum part-time.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 3 referees, should be sent to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 6th October, 1956.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time SENIOR CASUALTY OFFICER required at the Royal Infirmary, Doncaster. Salary within the range of £1575–£2025. Tenure for a period not exceeding 4 years.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 6th October, 1956.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Part-time CONSULTANT VENEREOLOGIST (Male) (1 half-day per week) at St. Helier Hospital, Carshalton, Surrey.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 6th October, 1956. Applicants may visit Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at Banstead Hospital, Sutton, Surrey. Candidates should have good psychiatric experience and possess D.P.M. An unfurnished house is available.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 6th October, 1956. Applicants may visit Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at Graylingwell Hospital, Chichester, Sussex. Candidates should have D.P.M. and wide experience in all branches of psychiatry. The post is for an experimental scheme for the extension of the domiciliary service and is being financed from non-Exchequer funds for a period of 2 years pending a review of the scheme. The successful candidate will be required to work in the Worthing area where the duties will include the treatment of patients at the Early Treatment Centre and at the Psychiatric Outpatients' Clinic and an active participation in the extension of domiciliary services in the district.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 6th October, 1956. Further particulars may be obtained from the Medical Superintendent, Graylingwell Hospital, Chichester.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time Locum Tenens ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at Park Prewett Hospital, Basingstoke, Hants (1675 Beds including Mental Hospital Annexes). Candidates must have D.P.M. and good experience in the diagnosis and treatment of mental illness. Period of appointment 24th September, 1956–10th January, 1957.

Applications, giving date of birth, qualifications, experience, and names of 3 referees, to the Group Secretary, Park Prewett Hospital Management Committee, Basingstoke, Hants, immediately.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at The Manor, Epsom, Surrey—a hospital with specialised facilities for the socio-industrial habilitation of high-grade mental defectives, and which has excellent facilities for research. Candidates should have D.P.M. Accommodation for a single person.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.I.), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 6th October, 1956. Applicants may visit Hospital by local arrangement.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens SENIOR HOSPITAL MEDICAL OFFICER ANÆSTHETIST required St. Tydfil's Hospital, Merthyr, for 1 month commencing 1st October, 1956.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

NEW ZEALAND. WAIKATO HOSPITAL, Hamilton, NEW ZEALAND. Applications are invited from qualified medical practitioners of the British Empire possessing a Diploma in Diagnostic Radiology for the following positions at the above Hospital.

SENIOR RADIOLOGIST to assume direction of Diagnostic X-ray Departments under the Board's control. Salary in accordance with the Hospital Employment Regulations and within the range of New Zealand £2000–New Zealand £2550, non-resident.

ASSISTANT RADIOLOGIST required for Diagnostic X-ray Department in the Waikato Hospital. Salary in accordance with the Hospital Employment Regulations and within the range of New Zealand £1600–New Zealand £1900, non-resident.

Conditions of appointment and form of application obtainable from the High Commissioner for New Zealand, 415, Strand, London, W.C.2. Applications close on 19th October, 1956.

A. C. BURGESS, Secretary.

Waikato Hospital Board, P.O. Box 934,
Hamilton, New Zealand.

WESTERN AUSTRALIA. ROYAL PERTH HOSPITAL.

SENIOR STAFF RADIOLOGIST.
STAFF RADIOLOGIST.

Applications are invited for the above full-time posts in Diagnostic Radiology. Candidates must be fully qualified Radiologists and preference will be given to those with higher qualifications.

Salary:

Senior Staff Radiologist: £A3100 p.a.

Staff Radiologist: Salary within the range of £A2360 p.a. to £A2540 p.a., according to qualifications and experience.

State Public Service Conditions, including superannuation, sick leave, &c.

The Royal Perth Hospital is a designated Medical Undergraduate Teaching Hospital; it has more than 600 Beds and is extending.

The Senior Staff Radiologist will work under the overall direction of the Director of Radiology who will be a senior member of the Honorary Staff. The Senior Staff Radiologist will be responsible for duties of full-time staff; internal management of the department; training of technicians; arrangement of demonstrations and provision of radiological teaching material.

A memorandum of further particulars concerning these posts will be supplied on request.

Applications must include particulars of qualifications, experience, age, marital status, war service if any, and the names of 2 referees, and should reach the undersigned on or before 30th September, 1956.

JOSEPH GRIFFITH, Administrator.

Hospital Services: Junior Appointments

ACTON HOSPITAL, Gunnersbury-lane, W.3. North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Part-time MEDICAL REGISTRAR required for 3 sessions per week for inpatient and outpatient duties. Post vacant 1st October, 1956. Ministry of Health conditions of service. Salary pro rata to whole-time scale.

Application forms obtainable from, and returnable to, Group Secretary, Central Middlesex Group Hospital Management Committee, Acton-lane, N.W.10, within 7 days.

ALBERT DOCK ORTHOPÆDIC AND FRACTURE HOSPITAL, Alnwick-road, E.16. SEAMEN'S HOSPITALS GROUP. SENIOR HOUSE OFFICER (surgery) required on 1st October. Post, which is normally resident, is recognised by the Royal College of Surgeons and provides excellent experience in a wide variety of traumatic conditions received from the adjacent dockland and from shipping in the Port of London. Salary £745 p.a.

Applications, stating age, nationality, qualifications and experience, with the names of 2 recent referees, should be sent to the Secretary, Dreadnought Seamen's Hospital, Greenwich, not later than 21st September.

CONNAUGHT HOSPITAL, Walthamstow, E.17. Locum RESIDENT ANÆSTHETIST required, 17th–28th September, inclusive. Registrar grade.

Apply Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (118 Beds.) Applications are invited for the post of SECOND CASUALTY OFFICER with duties in the Department of Orthopædic and Traumatic Surgery (Senior House Officer grade). Recognised for F.R.C.S. Salary £745 p.a., less £150 p.a. for board, lodging, &c.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Hospital Management Committee, Forest Group, Langthorne-road, E.11.

COLINDALE HOSPITAL, Colindale-avenue, London, N.W.9. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time MEDICAL REGISTRAR (resident or non-resident), required at above Hospital which accommodates 300 tuberculosis patients. Experience in diseases of the chest desirable. The Hospital, which is within easy access of the centre of London, may be visited by direct appointment with the Physician-Superintendent.

Application forms obtainable from, and returnable to, the Group Secretary, Edgware General Hospital, Edgware, by 25th September, 1956.

BETHLEM ROYAL HOSPITAL AND THE MAUDSLEY HOSPITAL. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER, commencing on 1st January, 1957, at the above Postgraduate Teaching Hospital, with which is associated the Institute of Psychiatry (University of London). Experience in general medicine and neurology or in the basic sciences is an advantage.

Applications, giving details of experience and the names of 2 referees, should be made within 1 week of the appearance of this advertisement. Application forms obtainable from K. J. JOHNSON, House Governor and Secretary, Maudsley Hospital Denmark-hill, London, S.E.5.

BETHLEM ROYAL HOSPITAL AND THE MAUDSLEY HOSPITAL. Applications are invited from registered medical practitioners for the appointment of SENIOR REGISTRAR (first year), commencing on 1st January, 1957, at the above Postgraduate Teaching Hospital, with which is associated the Institute of Psychiatry (University of London). Candidates should have a higher medical qualification, and experience in psychiatry is essential.

Applications, giving details of experience and the names of 2 referees, should be made within 1 week of the appearance of this advertisement. Application forms obtainable from K. J. JOHNSON, House Governor and Secretary, Maudsley Hospital, Denmark-hill, London, S.E.5.

BETHLEM ROYAL HOSPITAL AND THE MAUDSLEY HOSPITAL. Applications are invited from registered medical practitioners for the appointment of REGISTRAR, commencing on 1st January, 1957, at the above Postgraduate Teaching Hospital, with which is associated the Institute of Psychiatry (University of London). Candidates with experience in general medicine and neurology or in psychology will receive special consideration.

Applications, giving details of experience and the names of 2 referees, should be made within 1 week of the appearance of this advertisement. Application forms obtainable from K. J. JOHNSON, House Governor and Secretary, Maudsley Hospital, Denmark-hill, London, S.E.5.

DREADNOUGHT SEAMEN'S HOSPITAL, Greenwich, S.E.10. HOUSE PHYSICIAN (pre-registration) required on 4th October.

Applications, stating age, nationality, qualifications and experience with the names of 3 recent referees, should be sent to the Secretary at the above address not later than 24th September.

EAST END MATERNITY HOSPITAL, 394/396, Commercial-road, London, E.1. (58 Beds.) Applications are invited for the following posts which are recognised for the M.R.C.O.G.

RESIDENT SENIOR OBSTETRICAL OFFICER (Senior House Officer grade).

RESIDENT OBSTETRICAL OFFICER (House Officer, third post).

Posts vacant 1st November, 1956.

Applications, with copies of testimonials, to the Secretary, Stepney Group Hospital Management Committee, Raine-street, Wapping, E.1, by 24th September, 1956.

EASTERN HOSPITAL (Fevers), London, E.9. Registered RESIDENT HOUSE PHYSICIAN. Duties may include some work in Chest Unit. Facilities for postgraduate study for higher qualifications.

Applications to Group Secretary, Hackney Hospital, London, E.9, by 21st September, quoting EH/HO.

FULHAM CHEST CLINIC AND KING GEORGE V CHEST HOSPITAL, GODALMING. MEDICAL RESEARCH ASSISTANT (Registrar status) required for research project in chronic bronchitis to be carried out at the above Clinic and Hospital. Post will be held for 8 months in the first instance.

Applications (5 copies) to be submitted by 24th September, 1956, on forms obtainable from, and returnable to, Group Secretary (L.12.7.), Fulham and Kensington Hospital Management Committee, 5, Collingham-gardens, London, S.W.5.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. RESIDENT SURGICAL OFFICER (Registrar grading) required as soon as possible.

Applications, stating age, qualifications, experience, names of 2 referees, to Secretary, Board of Governors, by 22nd September.

HIGHLANDS GENERAL HOSPITAL, Winchmore-hill, London, N.21. SENIOR HOUSE OFFICER (resident for Chest Unit—100 Beds). Duties include tuberculosis work and investigation and treatment of chest diseases under supervision of the Finchley Chest Clinic.

Applications, with copies of 3 testimonials, to Hospital Secretary.

HIGHLANDS GENERAL HOSPITAL, Winchmore-hill, London, N.21. HOUSE PHYSICIAN, vacant 30th September, 1956. Preference given to applicants seeking pre-registration post under Medical Act, 1950.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. A vacancy occurs for RESIDENT SURGICAL OFFICER. Appointment for 6 months, with prospect of renewal. Post graded as Senior House Officer or Registrar, according to qualifications and previous surgical experience.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 26th September, 1956. THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. MEDICAL REGISTRAR (Cardiac Department). Applications are invited for this post, which is graded Registrar. Previous experience in cardiology and cardiac catheterisation desirable but not essential. The appointment is for 1 year with eligibility for reappointment.

Applications, stating date of birth and qualifications with dates, accompanied by copies of 3 testimonials, should reach the undersigned not later than 6th October, 1956.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

MILE END HOSPITAL, Bancroft-road, London, E.1. (484 Beds.) HOUSE PHYSICIAN (pre- or post-registration). Post vacant 18th October, 1956.

Application forms, obtainable from Physician-Superintendent, should be returned by 28th September, 1956, with copies of not more than 3 testimonials.

NORTH EAST METROPOLITAN REGIONAL HOS-PITAL BOARD AND BOARD OF GOVERNORS OF THE LONDON HOSPITAL, E.1. SENIOR REGISTRAR in Psychiatry required under Joint Training Scheme. Initially in Psychiatric Unit of 24 observation beds and 36 beds for treatment of neuroses and early psychoses at St. Clement's Hospital, Bow-road, E.3 (resident or non-resident). The Unit is run in conjunction with The London and Claybury Hospitals. Subsequent service at Runwell Hospital, near Wickford, Essex, and The London Hospital. Appointment subject to annual review.

Application forms from Secretary, North East Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, to be returned by 29th September.

PADDINGTON AND KENSINGTON CHEST CLINIC, 14/18, Newton-road, W.2. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR. Duties will include work at the Chest Clinic and at St. Charles' Hospital, W.9. A good medical background, preferably with higher degrees and some specialised knowledge of chest disease is required. Applicant required to take up duties as soon after 1st November as possible. Clinic can be visited by appointment.

Application forms obtainable from, and returnable to, Secretary, Paddington Group Hospital Management Committee, Paddington General Hospital, Harrow-road, W.9, by 1st October, 1956.

PRINCE OF WALES'S GENERAL HOSPITAL, N.15 Applications are invited from registered medical practitioners for the post of RESIDENT PÆDIATRIC HOUSE PHYSICIAN (third post) for a period of 6 months from 27th October, 1956. (Post recognised for D.C.H.)

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15, to be returned by 29th September, 1956.

QUEEN ELIZABETH HOSPITAL FOR CHILDREN MANAGEMENT COMMITTEE, Hackney-road, E.2, Shadwell, E.1, and BANSTEAD WOOD, SURREY. RESIDENT MEDICAL OFFICER (Male or Female), graded Senior House Officer at Banstead. Applications are invited for the above appointment vacant now. Candidates must have had experience in the treatment of sick children. The appointment will be for 1 year.

Application forms may be obtained from the Secretary at Hackney-road, and should be returned, with copies of not more than 3 testimonials, as soon as possible.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, London, E.15. HOUSE PHYSICIAN (third post) for 6 months commencing 6th November, 1956.

Applications, with copies of recent testimonials, to Hospital Secretary by 21st September, 1956.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, London, E.15. SENIOR CASUALTY OFFICER (Male or Female: Senior House Officer grade) for 1 year commencing as soon as possible after 1st October, 1956. Post recognised for F.R.C.S. (i.e., half the year is recognised as casualty and half as general surgery).

Applications, with copies of recent testimonials, to Group Secretary, West Ham Group Hospital Management Committee, Stratford, E.15, by 21st September, 1956.

ROYAL MARSDEN HOSPITAL, Fulham-road, S.W.3. Applications are invited for the post of SURGICAL SENIOR REGISTRAR to begin duty on 1st November, 1956. The appointment will be for 6 sessions. Candidates must hold the Diploma of F.R.C.S.

Applications, quoting the names of 3 referees, should be submitted by 1st October, on a form which may be obtained from the House Governor.

ROYAL MARSDEN HOSPITAL, Fulham-road, London, S.W.3. Applications are invited from registered medical practitioners for the post of HOUSE SURGEON (resident) to commence duty on 10th November, 1956. Salary £525 p.a. The post is tenable for 6 months.

Forms of application are obtainable from the House Governor, to whom applications, together with copies of 3 recent testimonials, should be sent not later than 8th October, 1956.

ROYAL MASONIC HOSPITAL, Ravenscourt Park, London, W.6. Applications are invited for the post of RESIDENT MEDICAL REGISTRAR. Appointment about 1st November. Gross salary: first year £850 (residential emoluments of £130 deductible); second year £965 (residential emoluments of £145 deductible).

Please state age, qualifications, past and present appointments and include 2 recent testimonials and/or the names of 2 referees. Applications should reach the undersigned (from whom further information may be obtained) as soon as possible, and in any event not later than 20th September.

R. E. LAWSON, Secretary and House Governor.

ROYAL EYE HOSPITAL, St. George's-circus, S.E.1. (KING'S COLLEGE HOSPITAL GROUP.) Applications are invited for the appointment of SENIOR HOUSE OFFICER (resident) with casualty duties. The appointment will be from 1st October, 1956, for 6 months in the first instance, but will be subject to reappointment.

Applications, stating age, education, qualifications and experience, with the names of 2 referees, should be sent to the undersigned by 22nd September, 1956.

S. W. BARNES, House Governor.

King's College Hospital, Denmark-hill, S.E.5.

ROYAL NATIONAL THROAT, NOSE AND EAR HOS-PITAL, Gray's Inn-road, W.C.1, and Golden-square, W.1. In association with The Institute of Laryngology and Otology. Applications are invited for a post of REGISTRAR or alternatively SENIOR HOUSE OFFICER. A higher surgical qualification is required for the former grading and at least the Primary F.R.C.S. for the latter. Considerable clinical experience in general surgery and in this specialty is required for either post. The appointment will be in accordance with the terms and conditions of service for the appropriate grade in the National Health Service.

Applications, giving full information and the names of 2 referees, should be sent to the House Governor by 1st October.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ANÆSTHETIC REGISTRAR required 1st December. Post recognised for D.A. and F.F.A.R.C.S.

Application forms, obtainable from Group Secretary, Wandsworth Hospital Group, at above address, to be completed and returned by 29th September.

ST. MARY'S HOSPITAL, Paddington, W.2. Applications are invited for the post of Part-time REGISTRAR to the E.N.T. Department for 2 notional half-days per week (Monday, P.M., Thursday, A.M.). The successful candidate will be required to take up his duties as soon as possible; remuneration to be at Registrar rates.

Applications, stating nationality, date of birth, permanent address, qualifications with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 25th September, 1956.

ST. MARY'S HOSPITAL, Paddington, W.2. Applications are invited from registered practitioners holding a Dental qualification, for the post of Whole-time NON-RESIDENT HOUSE OFFICER to the Dental Department (in new premises) under the direction of Sir Wilfred Fish and Mr. A. J. May. The appointment is for a period of 6 months in the first instance, as from a date to be arranged; remuneration to be at House Officer rates.

Applications, stating nationality, date of birth, permanent address, qualifications with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 25th September, 1956.

ST. NICHOLAS HOSPITAL, Plumstead, S.E.18. House OFFICER (Orthopædic, Fracture and Casualty Departments), vacant now. Recognised for F.R.C.S. 6 months resident post-registration appointment providing good general experience in a busy acute general hospital.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. NICHOLAS HOSPITAL, Plumstead, S.E.18. Senior HOUSE OFFICER (anæsthetics), vacant now. Recognised for F.F.A.R.C.S. and D.A. 6 months resident appointment and may be renewed.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. THOMAS'S HOSPITAL, London, S.E.1. Resident ASSISTANT PHYSICIAN (Senior Registrar grade), for a period of 1 year in the first instance from 15th February, 1957. Renewable for a second year.

Applications, naming 2 referees, to the Clerk of the Governors by 21st September, 1956.

ST. THOMAS'S HOSPITAL, London, S.E.1. Registrar to the Departments of Neurology and Psychiatry. For a period of 1 year in the first instance from 1st January, 1957. Some neurological experience essential.

Applications, naming 2 referees, to the Clerk of the Governors by 28th September, 1956.

ST. THOMAS'S HOSPITAL, London, S.E.1. Registrar to the Children's Department. For a period of 1 year in the first instance from 10th December, 1956.

Applications, naming 2 referees, to the Clerk of the Governors by 28th September, 1956.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy on 22nd November, 1956, for a RESIDENT ANÆSTHETIST (Registrar grade).

Full particulars, with form of application, which must be returned not later than Monday, 15th October, 1956, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

ST. STEPHEN'S HOSPITAL, Fulham-road, Chelsea, S.W.10. HOUSE PHYSICIAN (resident). General medicine and some tuberculosis. Vacancy 13th October, 1956.

Applications, naming 2 referees, to Medical Superintendent.

ST. LEONARD'S HOSPITAL, Nuttall-street, London, N.1. (Acute General—192 Beds.) Applications are invited from registered or provisionally registered medical practitioners for the post of HOUSE SURGEON. Post vacant 14th October, 1956.

Applications, with copies of 2 testimonials, to the Hospital Secretary by 21st September, 1956.

WESTMINSTER HOSPITAL, St. John's Gardens, S.W.1. Applications are invited for the post of RESIDENT MEDICAL OFFICER (Female) at Parkwood Auxiliary Hospital, Swanley, Kent, for 1 year in the first instance and renewable. Graded as Junior Hospital Medical Officer. A deduction of £170 p.a. will be made from the salary for board-residence. The post offers opportunity for study.

Applications (4 copies), with names of 2 referees, to House Governor.

WESTMINSTER HOSPITAL, St. John's Gardens, S.W.1. Applications invited for post of REGISTRAR to Radiological (Diagnostic) Department for 1 year in first instance from 5th November, 1956. Preference given candidates with a radiological diploma or a higher qualification in medicine or surgery.

Applications (6 copies), with names of 2 referees, to House Governor by 29th September.

WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1. Applications invited for post of Locum Tenens RESIDENT CASUALTY OFFICER (Senior House Officer grade) with duties as House Physician in Skin and V.D. Department from 1st October, 1956. Board and lodging £150 p.a.

Applications (2 copies), with names of 2 referees, to House Governor by 22nd September.

WHIPPS CROSS HOSPITAL, London, E.11. Applications are invited for the post of HOUSE PHYSICIAN (general medicine), post- or pre-registration, vacant 1st November, 1956.

Application forms from the Hospital Secretary to be returned by 24th September, 1956.

WOOLWICH GROUP HOSPITAL MANAGEMENT COMMITTEE.

OBSTETRICAL HOUSE OFFICER, British Hospital for Mothers and Babies, Samuel-street, Woolwich. Recognised for D.Obst.R.C.O.G. and M.R.C.O.G. Approved for Pre-registration Service. Vacant 1st November.

HOUSE SURGEON (gynæcology and obstetrics), Memorial Hospital, Shooters Hill, Woolwich. Recognised for M.R.C.O.G. (6 months gynæcology). Small Obstetric Unit providing good experience. Vacant early November.

Applications to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ALTON, HAMPSHIRE. LORD MAYOR TRELOAR ORTHOPÆDIC HOSPITAL. (340 Beds.) Applications are invited from SENIOR ORTHOPÆDIC REGISTRARS who desire a years experience in the same grade at a long-stay orthopædic hospital. Post includes attendance at peripheral clinics. Residence available.

Write to Secretary for application form.

ASHFORD HOSPITAL, Ashford, Middlesex. (560 Beds.) STAINES GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT HOUSE OFFICER (Male) for Special Departments. (E.N.T., paediatric, dermatology, &c.). 6 months appointment, vacant 1st November, 1956. Not suitable for pre-registration candidates; offers good experience before general practice.

Applications, stating age, qualifications and experience, with copies of up to 3 recent testimonials, to Medical Director of Hospital.

ASHFORD HOSPITAL, Ashford, Kent. Applications are invited for the appointment of SENIOR HOUSE SURGEON at the above Hospital. The appointment will be tenable for a year. Salary £745 a year, less a deduction of £150 a year for residential emoluments.

Applications, stating age, qualifications and the names and addresses of 2 referees, should be made to the Group Secretary, "Ash-Eton," Radnor Park West, Folkestone.

BANGOR. CAERNARVON AND ANGLESEY GENERAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (non-resident) in the Casualty Department of the above Hospital. Salary £745 p.a.

Applications, stating age, experience and nationality, together with the names and addresses of 2 referees, to be sent to the Group Secretary, Caernarvon and Anglesey Hospital Management Committee, Plas Gwyn, Ffriddoedd-road, Bangor, within 10 days of appearance of this advertisement.

BASINGSTOKE. PARK PREWETT HOSPITAL. South WEST METROPOLITAN REGION. Applications are invited for the immediate appointment of Locum Tenens PSYCHIATRIC REGISTRAR at above Hospital. The appointment is to the 31st December, 1956.

Applications, with full details of qualifications and experience, should be sent to the Group Secretary, Park Prewett Group Hospital Management Committee, Park Prewett Hospital, Basingstoke, as soon as possible.

BEDFORD GENERAL HOSPITAL. (439 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Locum GENERAL SURGICAL REGISTRAR required at above Hospital, 16th September, 1956.

Applications, giving full details of experience and names of 2 referees, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BEDFORD GENERAL HOSPITAL. (439 Beds.) House SURGEON required (mainly orthopædic). Pre- or post-registration; recognised for F.R.C.S. Vacant mid-October. Post offers exceptional opportunities for general experience in busy acute surgical units.

Inquiries and applications, with copies of 2 recent testimonials, to Group Secretary, 3, Kimbolton-road, Bedford.

BEDFORD GENERAL HOSPITAL. (439 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. GENERAL SURGICAL REGISTRAR (resident) required at above Hospital which may be visited by direct appointment. Post vacant October.

Application forms obtainable from, and returnable to, Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, as soon as possible.

BEDFORD GENERAL HOSPITAL. (439 Beds.) Senior HOUSE OFFICER in Medicine, now vacant, tenable for 12 months.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BEDFORD (near). BROMHAM HOSPITAL. (434 Beds for mental defectives and 60 at Annexe near Sandy.) REGISTRAR in Psychiatry required (resident). Hospital may be visited by direct appointment with the Medical Superintendent (phone: Oakley 295).

Application forms obtainable from, and returnable to, Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, by 17th September, 1956.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 Beds.) HOUSE PHYSICIAN (House Officer or Senior House Officer grading according to experience), vacant end of September. Pre-registration post but fully qualified practitioners may apply.

Applications to Group Secretary.

BRISTOL. WINFORD ORTHOPÆDIC HOSPITAL. (230 Beds.) SENIOR HOUSE OFFICER. Applications are invited from registered medical practitioners for this post. Vacant immediately. Suitable for candidate reading for higher grade qualifications and recognised for F.R.C.S. Hospital is staffed by Consultants of teaching hospitals.

Apply, stating age, qualifications and experience with testimonials, to Secretary.

BIRMINGHAM, 9. YARDLEY GREEN HOSPITAL. THORACIC SURGICAL UNIT. (66 Beds.) Vacancy for SENIOR HOUSE OFFICER. No previous experience in thoracic surgery necessary.

Applications, stating age, qualifications, training and experience, together with names of 2 referees, to be addressed to Group Secretary, Yardley Green Hospital, Birmingham, 9.

BIRMINGHAM, 13. SORRENTO MATERNITY HOS-PITAL, Wake Green-road. (106 Beds including 24 premature baby cots.) OBSTETRIC HOUSE SURGEON. Recognised for D.Obst.R.C.O.G. Hospital affiliated to Birmingham Medical School for training of students. Vacant 1st November.

Apply Obstetrician by 26th September.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. (780 Beds.) HOUSE SURGEON required. Recognised for pre-registration and F.R.C.S. Unit of approximately 85 adult and children's general surgical beds under control of 2 Consultant Surgeons.

Detailed applications, with copies of 3 recent testimonials, to Group Secretary.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. House PHYSICIAN (general medicine), vacant 1st November, 1956. Recognised for pre-registration. Responsible for approximately 80 male and female medical beds in a unit under control of 2 Consultant Physicians.

Applications, with copies of 2 recent testimonials, to the Group Secretary.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

(1) **Birmingham (Dudley Road) Group, Dudley Road Hospital, Birmingham, 18**

REGISTRAR (E.N.T. surgery) required at Birmingham and Midland Ear and Throat Hospital. Resident. Recognised for D.L.O. and F.R.C.S.

(2) **Birmingham Group 25, Oak Tree-lane, Birmingham, 29**

REGISTRAR (pathology) for Birmingham Accident Hospital. Vacant September. Previous experience essential. Recognised (12 months) for Diploma in Pathology. Further details from Consultant Pathologist.

(3) **Coventry Group, Coventry and Warwickshire Hospital, Coventry**

REGISTRAR (anæsthetics) for Coventry and Warwickshire and Gulson Hospitals. Experience specialty essential. Recognised F.F.A.R.C.S.

(4) **Mid-Worcestershire Group, Birmingham-road, Bromsgrove**

REGISTRAR (general surgery) for Kidderminster General Hospital. Experience specialty essential. Post recognised for F.R.C.S. Resident.

(5) **South Warwickshire Group, 50, Holly-walk, Leamington Spa**

REGISTRAR (psychiatry) for Coventry and South Warwickshire Groups. Outpatients (adults and children) at Coventry, Nuneaton, and Rugby Hospitals (7 sessions); 4 inpatients sessions at Central Hospital, near Warwick, with Neurosis Unit, E.E.G. Department, occupational therapy and all modern treatments. House or flat at Central Hospital.

(6) **Stoke-on-Trent Group, Princes-road, Stoke-on-Trent**

(*a*) REGISTRAR (orthopædics) for Biddulph Grange Orthopædic Hospital (104 children's beds). Resident. Considerable experience orthopædic and traumatic surgery available. Excellent library. Facilities for study. Possibility of married accommodation.

(*b*) REGISTRAR (chest diseases) for Cheshire Joint Sanatorium (305 Beds). Experience in general medicine required.

(*c*) REGISTRAR (E.N.T. surgery) for North Staffordshire Royal Infirmary. Experience specialty essential. Resident or non-resident.

Application forms from Group Secretaries, to be returned by 24th September.

BIRMINGHAM AND MIDLAND EAR AND THROAT HOSPITAL, Edmund-street, BIRMINGHAM, 3. SENIOR HOUSE OFFICER or HOUSE OFFICER (including pre-registration) required.

Apply to Group Secretary, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of a Locum SURGICAL REGISTRAR (Registrar grade) to the Surgical Professorial Unit at the Queen Elizabeth Hospital. The appointment will be for a period of up to 3 months with a possible extension. Candidates must have held a resident appointment and should hold at least a primary Fellowship qualification and will probably be required to be resident.

Forms of application from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, to be returned as soon as possible.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of NON-RESIDENT REGISTRAR (E.N.T. Department) for duties within the United Hospitals. Applicants should have had previous experience in the specialty and a higher qualification is desirable.

Forms of application may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, and should be returned not later than 29th September, 1956.

BISHOP'S STORTFORD. HERTS AND ESSEX GENERAL HOSPITAL. (Formerly Haymeads Hospital.) Applications are invited from registered medical practitioners for the appointment of a Whole-time Temporary SURGICAL REGISTRAR to commence 27th September, 1956, for 1 month in first instance followed by engagement on a week-by-week basis.

Applications, giving full details, together with copies of recent testimonials, or the names of referees, to the Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

BLACKPOOL. VICTORIA HOSPITAL. Senior House OFFICER required in the Department of Medicine for 1 year from 1st October, 1956.

Applications, stating age, qualifications and experience, should be sent to the Group Secretary, Blackpool and Fylde Hospital Management Committee.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, WESTBOURNE, HANTS. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER for E.N.T. and Ophthalmic duties. The appointment which becomes vacant on 22nd September, 1956, is recognised for the D.O. and D.L.O. Diplomas. In addition to duties at the above Hospital, the successful candidate will be required to assist in E.N.T. outpatient clinics at the Royal Victoria Hospital, Shelley-road, Bournemouth, and Poole General Hospital, Poole.

Applications to the Hospital Secretary, Royal Victoria Hospital, Shelley-road, Bournemouth.

BRENTWOOD, ESSEX. WARLEY HOSPITAL. Senior HOUSE OFFICER required. Hospital situated easy reach of London. Over 2000 Beds offering wide experience of all types of mental disorders (including the neuroses); all modern treatments carried out, including psychosurgery. Teaching by Senior staff, library and facilities for attending Postgraduate Courses. Experience in outpatient clinics. Regular clinical meetings held. Salary £745 p.a., less £150 for excellent residential amenities if required.

Applications, with full details and names of 2 referees, to Physician-Superintendent.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER in Pædiatrics. The post is based on Bury General Hospital, but will include duties at other hospitals in the Group. Post recognised for D.C.H.

Apply, stating age, qualifications, experience and names of 2 referees, to H. WILKINSON, Group Secretary,

Bury General Hospital, Bury, Lancs.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of PÆDIATRIC HOUSE PHYSICIAN, recognised for D.C.H., includes work in the ward and Outpatient Department and also provides experience in the care of the newborn. Opportunities exist for the study of preventive medicine among children and child guidance work. Post vacant at the end of September, 1956. National Health Service salary and conditions.

Applications, together with 2 testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of GENERAL SURGICAL AND ORTHOPÆDIC HOUSE SURGEON, which is recognised for the F.R.C.S. Diploma, is now vacant. National Health Service salary and conditions.

Applications, together with 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CHELTENHAM MATERNITY HOSPITAL. Cheltenham GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of RESIDENT OBSTETRIC OFFICER. The Hospital, which is recognised for the purpose of training for the D.Obst.R.C.O.G., has 50 Beds and deals with the majority of abnormal midwifery cases in North East Gloucestershire. The appointment is for a period of 6 months and the salary will be £425, £475, or £525 p.a., less £125 in respect of residential emoluments. The appointment will be vacant on 20th October, 1956.

Applications, stating age, qualifications, and experience, and accompanied by copies of 3 recent testimonials, should be sent to the Secretary, Cheltenham Group Hospital Management Committee, General Hospital, Cheltenham.

CARDIFF. GLAN ELY HOSPITAL, Fairwater, Cardiff. (240 Beds.) SENIOR HOUSE OFFICER (resident) required at above Hospital for treatment of pulmonary (Thoracic Unit) and all forms of non-pulmonary tuberculosis.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARDIFF HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER in Obstetrics and Gynæcology required. Appointment recognised for M.R.C.O.G.

Further particulars and form of application from Group Secretary, 44, Cathedral-road, Cardiff.

CARLISLE. GARLANDS HOSPITAL. (1060 Beds.) GARLANDS HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER at the above Mental Hospital. Salary £745 p.a. Flat is available for which a deduction will be made. Appointment is subject to the National Health Service superannuation regulations and to the conditions and terms of service laid down by the Minister of Health.

Applications, stating age, qualifications and experience, and the names of 2 referees, should be sent to the Medical Superintendent as soon as possible.

CARSHALTON, SURREY. ST. HELIER HOSPITAL. HOUSE SURGEON (approved pre-registration post), vacant end October.

Applications, stating age, qualifications and experience, with copies of recent testimonials and the names of 2 referees, should be sent to the Secretary at above address.

CARSHALTON, SURREY. ST. HELIER HOSPITAL. (711 Beds.) Whole-time SENIOR THORACIC MEDICAL REGISTRAR (non-resident).

Candidates who have sound experience in thoracic medicine can obtain application forms from the Group Secretary at the above address (returnable by 29th September, 1956).

CHEPSTOW, MONMOUTHSHIRE. ST. LAWRENCE HOSPITAL. (127 plastic surgery, 50 orthopædic beds.) PLASTIC SURGERY, JAW INJURIES AND BURNS CENTRE. SENIOR HOUSE OFFICER in Plastic Surgery required. Previous experience in specialty not essential. The Hospital intakes from most of Wales and the successful candidate will receive a thorough training. There is a second Senior House Officer in plastic surgery and also a Senior House Officer in orthopædics, Senior Registrar, non-resident, and 2 Registrars, all in plastic surgery, resident. Salary £745, less £150 board-residence.

Write, quoting 2 referees, to T. A. JONES, Group Secretary.

64, Cardiff-road, Newport, Mon.

CHESTER ROYAL INFIRMARY. Applications are invited for the post of RESIDENT CASUALTY OFFICER (Junior Hospital Medical Officer). The post is recognised for the F.R.C.S.

Applications, giving full details, together with the names and addresses of 2 referees, should be forwarded to the Group Secretary, Chester and District Hospital Management Committee, 5, King's-buildings, Chester.

CHESTERFIELD ROYAL HOSPITAL. Senior House OFFICER required 1st October at above Hospital for Accident and Orthopædic Department. Post recognised for F.R.C.S. training and offers valuable experience. National salary and conditions.

Apply M. H. BOONE, Secretary, Chesterfield Hospital Management Committee.

CLACTON AND DISTRICT HOSPITAL, Clacton-on-Sea. (58 Beds.) Applications invited for post of SENIOR HOUSE OFFICER (Resident Surgical Officer). Post tenable for 1 year.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

COATBRIDGE, AIRDRIE AND DISTRICT HOSPITALS BOARD OF MANAGEMENT. Applications are invited for the following RESIDENT JUNIOR HOSPITAL MEDICAL OFFICER posts :—

(*a*) For duty in Tuberculosis Wards and Thoracic Unit at Hairmyres Hospital, East Kilbride.

(*b*) To undertake the immediate medical supervision of the following hospitals :—

Lightburn I.D. Hospital and Sanatorium, Shettleston.

Coathill Hospital, Coatbridge (I.D. and Geriatric patients).

The resident accommodation in the case of (*b*) is located at Lightburn Hospital.

Both appointments are subject to the provisions of the National Health Service superannuation scheme. Salary scale £775–£1075 p.a.

Applications, stating age and nationality and giving details of training, qualifications and experience, together with the names of not more than 3 referees, should be lodged as soon as possible with the Group Secretary, Hairmyres Hospital, East Kilbride.

COLCHESTER. ESSEX COUNTY HOSPITAL. (188 Beds.) Applications invited for post of SENIOR HOUSE OFFICER to Casualty and E.N.T. Departments. Post tenable for 6 months or 1 year. Recognised for F.R.C.S.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

CROYDON. ST. MARY'S MATERNITY HOSPITAL. (33 Beds.) CROYDON GROUP HOSPITAL MANAGEMENT COMMITTEE. OBSTETRIC HOUSE SURGEON (resident). Post recognised for D.Obst.R.C.O.G., vacant from 22nd September, 1956.

Application forms obtainable from GEORGE A. PAINES, Secretary, Hospital Management Committee, General Hospital, Croydon.

FARNBOROUGH HOSPITAL, Kent. (800 Beds.) Ortho-PÆDIC SENIOR HOUSE OFFICER required for 1 year from 1st October. Recognised for F.R.C.S. Deduction for residence £150.

Apply, stating age, qualifications with dates, and experience, and naming 3 referees, to Administrative Officer.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. MEDICAL REGISTRAR, Papworth Hospital, Cambridgeshire. Post provides good experience in tuberculosis and other chest diseases. Appointment for 1 year, renewable for second year.

Applications, stating age, experience and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 24th September, 1956. Candidates invited to visit Hospital by direct arrangement with Physician-Superintendent.

EDINBURGH CENTRAL HOSPITALS. Applications are invited from registered medical practitioners for the appointment of ANÆSTHETIST (Junior Hospital Medical Officer grade), commencing 1st October, 1956. Salary scale £775–£1075. National Health Service conditions. Non-resident. Work mainly with children but includes some adult general surgery and gynæcology.

Applications, with full particulars of age, qualifications and experience, and names of 2 referees, to be submitted immediately to Medical Superintendent, Edinburgh Central Hospitals, 18, Rillbank-terrace, Edinburgh, 9.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. ENFIELD GROUP HOSPITAL MANAGEMENT COMMITTEE. Appointment of RESIDENT HOUSE PHYSICIAN (third post), vacant 8th November, 1956. General medical duties. 6 months appointment.

Applications, with the names of 2 referees, to the Secretary, Enfield Group Hospital Management Committee, by 29th September, 1956.

EPPING. ST. MARGARET'S HOSPITAL. (480 Beds.) RESIDENT SENIOR HOUSE OFFICER. Post vacant 1st November, 1956. Required for Chest Department and to act as Second Resident Anæsthetist. Good opportunity for experience in modern methods. Previous experience in chest diseases desirable but not essential.

Applications, with references, to reach Group Secretary, Epping Group Hospital Management Committee, "Oak Cottage," The Plain, Epping, Essex, by 28th September.

EPPING. ST. MARGARET'S HOSPITAL. (480 Beds.) RESIDENT SENIOR HOUSE OFFICER (surgery) as Casualty Officer and Orthopædic House Surgeon. Post vacant 1st October, 1956. Recognised training post for F.R.C.S. Busy general hospital with easy access to London. Salary on national scale, less deduction for board, lodging, &c.

Applications, with copies of 2 recent testimonials, to the Group Secretary, Epping Group Hospital Management Committee, "Oak Cottage," The Plain, Epping, Essex.

EPSOM GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for Whole-time REGISTRAR in Chest Medicine to the Epsom and Dorking Chest Clinics. Vacancy 1st December, 1956. Duties will include sessions at 1 or both clinics. Additionally, person appointed will be Registrar at Cheam Sanatorium where there are 53 Beds for the treatment of cases of pulmonary tuberculosis, and will have the day-to-day care of patients under the various Consultants concerned. Successful candidate will be required to live within easy access of Cheam Sanatorium. Applicants may visit Units by arrangement with Consultant Chest Physician.

Application forms may be obtained from Group Secretary, Epsom District Hospital, Dorking-road, Epsom (send stamped addressed foolscap envelope), for completion and return within 14 days.

GRIMSBY GENERAL HOSPITAL. Grimsby Hospital MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (orthopædic). Orthopædic Unit of 74 Beds. Resident establishment—Registrar and 2 House Officers. Up-to-date Medical Library and reading facilities available.

Applications, with names of 2 referees, to Hospital Secretary.

GRIMSBY. GENERAL HOSPITAL. (Recognised for training for F.F.A.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT or RESIDENT (single accommodation only) REGISTRAR (anæsthetics) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 24th September, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

GLOUCESTER. HORTON ROAD AND CONEY HILL HOSPITALS. (1450 Beds.) Applications invited for the appointment of a JUNIOR HOSPITAL MEDICAL OFFICER. Hospital serves the North Gloucestershire Clinical Area including Gloucester, Cheltenham, Stroud and Forest of Dean. High admission-rate (800). All modern methods of treatment. New units provided for treatment of neurosis and alcoholism. Expanding outpatient services, long-stay annexes, and social clubs. Encouragement and opportunity for study. Salary and conditions Whitley Council. Single accommodation available. Married accommodation a possibility.

Applications, with names of 3 referees, to Physician-Superintendent within 14 days.

GLASGOW NORTHERN HOSPITALS BOARD OF MANAGEMENT. Applications are invited for the post of SENIOR HOUSE OFFICER in Pathology and Hæmatology at Stobhill General Hospital, Glasgow. The appointment will be for 1 year in the first instance.

Applications, stating age, qualifications, experience and present appointment, and naming 2 referees, to be lodged with the Secretary, 13, Woodside-place, Glasgow, C.3, by 19th September, 1956.

GLASGOW, S.W.1. SOUTHERN GENERAL HOSPITAL. SENIOR HOUSE OFFICER in Anæsthetics. The post is approved for D.A.

Write immediately to Secretary, Board of Management for Glasgow South-Western Hospitals, 1301, Govan-road, Glasgow, S.W.1, naming 2 referees.

GLASGOW, N.1. STOBHILL GENERAL HOSPITAL. Applications are invited for the post of HOUSE OFFICER in Anæsthetics and should be addressed to the Medical Superintendent, giving the names of 2 referees.

GLASGOW, N.1. STOBHILL GENERAL HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER in the Pulmonary Tuberculosis Unit (31 Beds) with an attachment to the associated chest clinic. There are ample opportunities for the study of all forms of chest disease and general medical cases.

Applications, stating age, qualifications and experience, with the names of 2 referees, to be sent to the Medical Superintendent.

HARROGATE AND DISTRICT GENERAL HOSPITAL. (253 Beds. Recognised for D.Obst.R.C.O.G.) Applications are invited for the resident post of SENIOR HOUSE OFFICER in Obstetrics and Gynæcology, vacant 1st November.

Applications, naming 2 referees, should reach the Hospital Secretary, Harrogate and District General Hospital, Harrogate, Yorks, by 25th September.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) HOUSE SURGEON (pre-registration post), vacant now. National scale of salary.

Apply to Hospital Administrator.

HEREFORDSHIRE GROUP. Registrar in General Surgery. Duties mainly at General (154 Beds—71 surgical beds including fracture and orthopædic) and County Hospitals, Hereford (335 Beds—40 surgical). Recognised for F.R.C.S. Resident.

Application forms from Group Secretary, Victoria House, Eign-street, Hereford, to be returned before 1st October, 1956. Candidates may visit hospitals.

HOVE GENERAL HOSPITAL, Sussex. (75 Beds. 3 Resident Medical Officers.) Pre-registration HOUSE PHYSICIAN required 28th October, 1956. Excellent clinical material available. Post is suitable for candidate working for higher degree. Salary £425–£525, less £125 p.a. for residential emoluments.

Applications, stating age, qualifications, full details of experience, together with the names and addresses of 2 referees, to the Administrative Officer.

HITCHIN, HERTFORDSHIRE. LISTER HOSPITAL. Applications are invited for the post of RESIDENT HOUSE SURGEON, vacant 16th October, 1956. Recognised as pre-registration post and for F.R.C.S.

Applications, stating age, nationality, qualifications, and experience, together with copies of 3 recent testimonials, to be sent to the Medical Administrator as soon as possible.

HITCHIN. LISTER HOSPITAL. (317 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time MEDICAL REGISTRAR required at above Hospital. Post gives good all-round experience, valuable for the M.R.C.P. Vacant 22nd November, 1956. Hospital may be visited by direct appointment.

Application forms obtainable from the Secretary, Luton and Hitchin Group Hospital Management Committee, St. Mary's Hospital, Luton, Beds, and returnable by 24th September, 1956.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT JUNIOR HOUSE SURGEON (pre- or post-registration). Recognised for the F.R.C.S. examinations. Busy acute General Surgical Unit. Vacant 1st October.

Applications, with 2 recent testimonials, to the Hospital Secretary.

HUNTINGDON COUNTY HOSPITAL. Applications are invited for the post of HOUSE OFFICER (medical). Post recognised for pre-registration purposes. The selected candidate will be required to look after medical and paediatric cases and may be called upon to give emergency anæsthetics. Post vacant beginning of October.

Apply, with full particulars and names of 2 referees, to Secretary, County Hospital, Huntingdon.

ISLE OF MAN. BALLAMONA HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER at the above Mental Hospital (350 Beds, admission-rate 200 annually), which undertakes all modern methods in the treatment of mental and nervous diseases as well as mental deficiency, and is recognised for training for the Conjoint D.P.M. A choice of 2 furnished flats is available. The terms and conditions of service are those of the Isle of Man Health Service, the same as those of the National Health Service. Superannuation is transferable. The Hospital may be visited by appointment.

Those interested should write for further details, and applications, stating age, nationality, qualifications and experience, together with the names of 2 referees, should be sent to the Medical Superintendent.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Locum ANÆSTHETIC SENIOR REGISTRAR required for 3 months from 24th September, 1956, whilst present Senior Registrar is away on special course.

Applications to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 20th September.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-ON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified and experienced medical officers for the post of SENIOR HOUSE OFFICER (orthopædic and casualty). The post, which is available on 1st October, 1956, is recognised in casualty for F.R.C.S. purposes.

Applications, stating age, qualifications, and experience, with 2 testimonials, should reach the Physician-Superintendent of the Hospital by 22nd September, 1956.

KETTERING GENERAL HOSPITAL, Kettering. (170 Beds.) Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER in Anæsthetics. Post recognised for D.A.

Applications, giving details of qualifications and experience, and enclosing copies of 3 recent testimonials, to be sent to the Group Secretary, Kettering and District Hospital Management Committee, at the above address.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies.

Anæsthetics

Huddersfield Group (approximately 225 Beds in the Surgical Specialties). Non-resident.

General Surgery

Pinderfields General Hospital (70 general surgical beds). Resident—possibility of married accommodation. Recognition of post by the Royal College of Surgeons applied for.

Infectious Diseases

Castle Hill Hospital, Cottingham (167 infectious diseases beds). Resident.

Psychiatry

(i) Clifton Hospital, York (1100 Beds). Resident or non-resident.

(ii) Stanley Royd Hospital, Wakefield (1976 Beds).

If desired facilities for attending Leeds University will be provided if the successful candidates are studying for the D.P.M.

Applications, stating age, qualifications, and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 28th September, 1956.

LEEDS. THE UNITED LEEDS HOSPITALS. The GENERAL INFIRMARY AT LEEDS. SENIOR HOUSE OFFICER in E.N.T. Department required for a period of 6 months from 1st November, 1956. The appointment will be renewable for a further period of 6 months. Terms and conditions of service for hospital medical staff apply.

Applications, giving details of age, qualifications, posts held with dates, and with 3 names for reference, should be sent to the Secretary to the Board as soon as possible.

LEEDS. THE UNITED LEEDS HOSPITALS. The GENERAL INFIRMARY AT LEEDS. SENIOR HOUSE OFFICER in Neurosurgery required for a period of 6 months from 1st November, 1956. The appointment will be renewable for a further period of 6 months. Terms and conditions of service for hospital medical staff apply.

Applications, giving details of age, qualifications, posts held with dates, and with 3 names for reference, should be sent to the Secretary to the Board as soon as possible.

LEEDS. THE UNITED LEEDS HOSPITALS. The GENERAL INFIRMARY AT LEEDS. HOUSE OFFICER (Senior or Junior—pre- or post-registration) required for Department of Urology. Post tenable for 6 months from 1st November, 1956. Salary according to grade. Terms and conditions of service for hospital medical staff apply.

Applications, stating age, qualifications, previous posts with dates, and 3 names for reference, to be sent to the Secretary to the Board as soon as possible.

LEEDS. THE UNITED LEEDS HOSPITALS. The GENERAL INFIRMARY AT LEEDS. RESIDENT RADIOTHERAPY OFFICER (Senior House Officer status). The appointment is for a period of 6 months in the first instance, commencing 1st November, 1956. The post affords facilities for training for D.M.R.T. Conditions of service for hospital medical staff apply.

Applications, stating age, qualifications, previous posts with dates, and 3 names for reference, should be sent to the Secretary to the Board as soon as possible.

LEEK (near). ST. EDWARD'S HOSPITAL, Cheddleton, near LEEK, STAFFS. JUNIOR HOSPITAL MEDICAL OFFICER. Previous mental hospital experience not essential. This Hospital offers opportunities for gaining experience in all branches of psychiatry. Terms and conditions of service will be as approved for hospital medical staff employed in the National Health Service. Salary £775–£50–£1075. Single furnished quarters or unfurnished house on Hospital estate available for a married man.

Applications as soon as possible to the Medical Superintendent.

LEICESTER ROYAL INFIRMARY. Applications are invited for the posts of SENIOR HOUSE OFFICER (pathology) (2) vacant 1st October. The posts are recognised for D.Path. and D.C.P.

Applications, stating age, qualifications, and experience, together with copies of recent testimonials, to the Group Secretary, No. 1 Hospital Management Committee, The Leicester Royal Infirmary, forthwith.

LINCOLN COUNTY HOSPITAL. (200 Beds.) Sheffield REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (pædiatrics) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 24th September, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

MACCLESFIELD AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER in Surgery. Pre-registration post. Acute Surgical Unit of 100 Beds. Recognised for F.R.C.S purposes. Main casualty duties undertaken by Senior Resident Practitioner.

Apply immediately to Group Secretary, "Willerby House," Cumberland-street, Macclesfield.

MANCHESTER (near). ALTRINCHAM GENERAL HOSPITAL, ANNEXE AND E.N.T. DEPARTMENT. (183 Beds.) SENIOR HOUSE OFFICER (medical). This appointment is in a busy hospital and offers excellent opportunities of practical experience. Post vacant end of September.

Applications, together with 2 recent testimonials, to Group Secretary, North and Mid-Cheshire Hospital Management Committee, The Hospital, Sinderland-road, Altrincham, Cheshire.

MANCHESTER (near). ALTRINCHAM GENERAL HOSPITAL. ASSISTANT SENIOR SURGICAL OFFICER (Junior Hospital Medical Officer grade). Applications are invited for this post in a hospital of 130 acute beds with a busy Casualty Department. The appointee would be required to exercise control of this Department and also to assist Resident Surgical Officer with the general surgical work of the Hospital. The post offers excellent opportunities of practical experience and postgraduate study to suitably qualified candidates and particularly those studying for higher surgical qualifications.

Applications, with names of 2 referees, to Group Secretary, North and Mid-Cheshire Hospital Management Committee, Sinderland-road, Altrincham.

MANCHESTER, 20. CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER (radiotherapy) at the above Hospital, commencing in October, 1956. Training will be available from April, 1957, for Diploma in Radiotherapy Course.

Applications, with full details, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, immediately.

MANCHESTER REGIONAL HOSPITAL BOARD. SALFORD HOSPITAL MANAGEMENT COMMITTEE. Applications invited for post of REGISTRAR in Obstetrics and Gynæcology, Hope Hospital, vacant 30th October, 1956. Hospital recognised for M.R.C.O.G.

Applications, together with names and addresses of 2 referees, to be sent to Group Secretary, Salford Royal Hospital, Salford, 3, before 22nd September, 1956.

MANCHESTER REGIONAL HOSPITAL BOARD invites applications for post of RESIDENT SURGICAL REGISTRAR to Macclesfield District Group Hospitals, main duties Infirmary Branch Macclesfield Hospital. Hospital recognised for F.R.C.S. regulations.

Apply immediately, with names and addresses of 2 referees, to Group Secretary, "Willerby House," Cumberland-street, Macclesfield.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. PARK HOSPITAL, DAVYHULME. (General Hospital—433 Beds.) 1 SENIOR HOUSE OFFICER (non-tuberculous Thoracic Surgery) required for Manchester Regional Hospital Board Centre. Post now vacant.

Form from Secretary.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. PARK HOSPITAL, DAVYHULME. (General Hospital—433 Beds.)

HOUSE OFFICER (general medicine) required. Pre-registration. Post vacant middle October.

HOUSE OFFICER (obstetrics) required. Pre-registration. Post recognised for M.R.C.O.G. examination. Post vacant middle October.

3 HOUSE OFFICERS (general surgery) required. Pre-registration. Posts recognised for F.R.C.S. examination. Vacant mid-October, end-October, mid-November respectively.

Application forms from Secretary.

MANCHESTER, 23. WYTHENSHAWE HOSPITAL. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of CASUALTY OFFICER (Senior House Officer grade) at Wythenshawe Hospital. This post is recognised by the Royal College of Surgeons.

Applications, stating age, qualifications, present post, and names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, within 7 days of the appearance of this advertisement.

MARGATE. GENERAL HOSPITAL. (132 Beds.) Senior HOUSE OFFICER (surgical). Recognised for F.R.C.S. and D.A. Salary £745 p.a., less charge for residential emoluments.

Applications, with copies of testimonials, to Hospital Secretary.

MAIDENHEAD HOSPITAL, Berkshire. Applications invited from registered practitioners for post of HOUSE PHYSICIAN, vacant 22nd September.

Applications, stating age, qualifications, experience and nationality, with names of 3 referees, to Secretary.

NORTHAMPTON GENERAL HOSPITAL. (482 Beds.) Vacancies 1st October, 1956, for the following :—

HOUSE OFFICER (general surgery); recognised for F.R.C.S.
HOUSE OFFICER (Department of Anæsthetics); recognised for D.A.
HOUSE OFFICER (Pædiatric Department); recognised for D.C.H.
HOUSE OFFICER (Fracture and Orthopædic Department); recognised for F.R.C.S.
HOUSE OFFICER (Casualty Department); recognised for F.R.C.S.
SENIOR HOUSE OFFICER (Casualty Department); recognised for F.R.C.S.
SENIOR HOUSE OFFICER (E.N.T. Department); recognised for F.R.C.S. and D.L.O.
SENIOR HOUSE OFFICER (Department of Pathology).

All posts, except those of Anæsthetic House Officer and the Senior House Officer posts, recognised for pre-registration. Casualty House Officer and Pædiatric House Officer posts recognised for medical pre-registration. All 6 months appointments in first instance.

Applications, enclosing copies of 3 testimonials, as soon as possible, to S. G. HILL, Superintendent.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER (casualty) duties to commence on or about 7th September, 1956. Establishment 3. Recognised for F.R.C.S. Post offers wide experience of casualty work.

Applications, stating age, nationality, qualifications and experience, together with copies of testimonials, to be sent to the Secretary, General Hospital, Nottingham.

NOTTINGHAM. HIGHBURY HOSPITAL. Senior HOUSE OFFICER (surgical) required at the above Hospital. Good opportunity for obtaining experience in all types of general surgery. Duties to commence on or about 16th September, 1956.

Applications, stating age, qualifications and experience, and nationality, together with copies of testimonials, to be sent to the Group Secretary, General Hospital, Nottingham.

NORWICH. ST. ANDREW'S HOSPITAL, Thorpe, NORWICH. Applications are invited from registered medical practitioners (Male or Female) for the appointment of SENIOR HOUSE OFFICER (psychiatric). The Hospital has 1250 Beds, an admission rate of over 600 annually and affords comprehensive experience in psychiatry. The salary and conditions of service will be as laid down by the Ministry for Senior House Officers. Residential accommodation with board available.

Applications, stating age, qualifications and full particulars of experience, together with the names and addresses of 2 referees, to be sent as soon as possible to the Medical Superintendent.

NEWCASTLE REGIONAL HOSPITAL BOARD. Gateshead HOSPITAL MANAGEMENT COMMITTEE. REGISTRAR PHYSICIAN (whole-time), resident, at Bensham General Hospital (386 Beds).

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Gateshead DISTRICT HOSPITAL MANAGEMENT COMMITTEE. QUEEN ELIZABETH HOSPITAL (176 Beds); BENSHAM GENERAL HOSPITAL (386 Beds). SENIOR REGISTRAR RADIOLOGIST (whole-time). Single accommodation available.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 21 days.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the non-resident appointment of REGISTRAR in the Department of Radiotherapy at the Royal Victoria Infirmary. The appointment will be for 1 year in the first instance and subject to the terms and conditions of service of hospital medical staff. Opportunities will be given for study for the D.M.R.T.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NEWMARKET GENERAL HOSPITAL, Suffolk. Applications are invited for the post, now vacant, of SENIOR HOUSE OFFICER, for orthopædic and casualty duties. The post is resident.

Applications, giving age, nationality and qualifications, together with 3 recent testimonials, should be sent to the Medical Superintendent.

NUNEATON. MANOR HOSPITAL. (125 Beds.) Receiving ROOM OFFICER for casualty duties. Resident, furnished flat available. Junior Hospital Medical Officer status. Recognised F.R.C.S.

Applications to Hospital Secretary.

NUNEATON. MANOR HOSPITAL. (125 Beds.) House OFFICER (pre-registration), General Surgery. Recognised F.R.C.S. Resident.

Applications to Hospital Secretary.

NUNEATON. MANOR HOSPITAL. (125 Beds.) House OFFICER (orthopædic and general surgery), pre-registration (60 Beds). Resident.

Applications to Hospital Secretary.

OXFORD REGIONAL HOSPITAL BOARD. Registrar (whole-time) in Diseases of the Chest to the hospitals and clinics of the Aylesbury/High Wycombe Hospital Management Committees. The appointment will be for 1 year and eligible for extension for a second year. The successful candidate will be required to live in the area.

Applications, on forms obtainable from the Secretary, Committee for Registrars, 43, Banbury-road, Oxford, should reach him by 25th September, 1956.

OXFORD REGIONAL HOSPITAL BOARD. Registrar (part-time) in Dermatology for 7 sessions a week, to the Departments in the Aylesbury and High Wycombe area.

Application forms from the Secretary, Committee for Registrars, 43, Banbury-road, Oxford, to reach him by 1st October.

OXFORD REGIONAL HOSPITAL BOARD. Registrar (whole-time) in Psychiatry, to St. Crispin Hospital, Duston, Northamptonshire. There is excellent opportunity to gain experience in adult and child psychiatry, inpatient and outpatient work, and E.E.G. Unit. Post recognised for D.P.M. Residential accommodation for married or single applicant.

Application forms, obtainable from the Secretary, Committee for Registrars, 43, Banbury-road, Oxford, should reach him by 6th October.

OXFORD. UNITED OXFORD HOSPITALS. Applications are invited for the post of HOUSE SURGEON in the Thoracic Surgery Unit at the Churchill Hospital, to commence as early as possible until 31st January, 1957.

Applications, stating age, qualifications and experience, together with names of 2 referees, to Administrative Assistant, Radcliffe Infirmary, Oxford.

PAISLEY. RICCARTSBAR HOSPITAL. Junior Hospital MEDICAL OFFICER required. The Hospital is of approximately 350 Beds and has a very active Inpatient and Outpatient Department including child guidance. It is recognised for the D.P.M., London University, London Conjoint and R.M.P.A. Facilities are available for attending classes at Glasgow University. The post may be resident or non-resident.

Applications should be addressed to the Physician-Superintendent at an early date.

PETERBOROUGH. THE MEMORIAL HOSPITAL AND OBSTETRIC ANNEXES. PETERBOROUGH AND STAMFORD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON (obstetrics and gynæcology). Applications are invited for vacancy on 28th October, 1956. Busy Gynæcological Department and 54 obstetric beds. Unit consists of a Consultant, Registrar and 2 House Surgeons. Recognised for D.Obst.R.C.O.G.

Application forms from Secretary.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL.

HOUSE SURGEON (pre-registration post), vacant 1st December, 1956. Recognised for the F.R.C.S. Devonport Section.

HOUSE SURGEON (pre-registration post), vacant 1st December, 1956. Recognised for the F.R.C.S. Greenbank Road Section.

Applications, stating age, nationality, qualifications and experience, together with the names and addresses of 3 referees, to be sent to—

ARTHUR R. CASH, Group Secretary, Plymouth.
South Devon and East Cornwall General Hospital Group.
7, Nelson-gardens, Stoke, Plymouth.

PLYMOUTH. MOUNT GOLD HOSPITAL. Senior HOUSE OFFICER for the Orthopædic and Fracture Service centring on Mount Gold Orthopædic, with annexe (122 Beds) and associated Hospitals. Post recognised by R.C.S.

Applications, stating age, qualifications with dates, &c., and with copies of 2 recent testimonials, to be forwarded to the Secretary within 14 days of this advertisement appearing.

PONTEFRACT GENERAL INFIRMARY. House Surgeon required. Married accommodation available. This is an approved pre-registration post under Medical Act, 1950, but applications will be considered from fully registered practitioners. Hospital approved under F.R.C.S. regulations, and provides excellent surgical experience.

Apply to the Secretary, Pontefract and Castleford Hospital Management Committee, Great Northern House, Salter-row, Pontefract, Yorkshire.

POOLE GENERAL HOSPITAL, Longfleet-road, Poole, DORSET. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. CASUALTY OFFICER (Senior House Officer) required immediately. Resident or non-resident. Hours of duty 9 A.M.–6 P.M. Post suitable for person reading for higher diplomas.

Applications, with copies of 2 recent testimonials, to the Hospital Secretary.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

(1) **Queen Alexandra Hospital**
SENIOR HOUSE SURGEON (recognised for the F.R.C.S.) (87 surgical beds), vacant now.

(2) **Royal Portsmouth Hospital**
(*a*) SENIOR HOUSE SURGEON (recognised for the F.R.C.S.) (70 surgical beds) vacant 19th September, 1956.
(*b*) ANÆSTHETIST (Senior House Officer grade). Recognised for the F.F.A.R.C.S. Vacant 1st October, 1956.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST.

St. Mary's Hospital, Milton-road, Portsmouth.

READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER in the Area Department of Diseases of the Chest, for duty in the Reading Chest Clinic. The post offers wide experience in both tuberculous and non-tuberculous chest diseases and duties will include attendance at Prospect Park Hospital, Reading, and Peppard Chest Hospital, Henley. Facilities are available for postgraduate studies. Salary within the scale £775–£1075 p.a.

Applications, stating age and qualifications, together with names of 3 referees, should be sent to the Group Secretary, 3, Craven-road, Reading.

READING AREA HOSPITALS. Applications are invited for the post of SENIOR HOUSE OFFICER (pathology). Previous experience in pathology desirable, but not essential. Salary £745, less £150 board-residence.

Apply, stating age, qualifications with dates, nationality, present post, together with the names of 3 referees, to Group Secretary, 3, Craven-road, Reading.

READING. BATTLE HOSPITAL. (391 Beds.) Applications are invited from registered medical practitioners for the post of RESIDENT JUNIOR HOUSE SURGEON in the Area Accident and Orthopædic Department. Post vacant 1st October next. F.R.C.S. recognised. Also casualty duties. Salary £425–£525 p.a., less £125 board-residence.

Apply, stating age, qualifications with dates, nationality, present post, with 1 copy of recent testimonial, to Hospital Secretary.

READING COMBINED HOSPITALS. Area Department OF OBSTETRICS AND GYNÆCOLOGY. (104 Beds.) Applications are invited from registered medical practitioners, Male and Female, for the resident appointment of GYNÆCOLOGICAL HOUSE SURGEON at the Royal Berkshire Hospital, Reading. Vacant 1st October and tenable for 6 months. Post recognised for M.R.C.O.G.

Write, stating age and qualifications with dates, nationality, and present appointment, with copy of 1 recent testimonial, to Secretary.

REDHILL. EAST SURREY HOSPITAL, Shrewsbury-road, REDHILL. RESIDENT HOUSE SURGEON (pre-registration appointment), vacant late September.

Apply Hospital Secretary, naming 2 referees.

RUGBY. HOSPITAL OF ST. CROSS. (168 Beds.) HOUSE OFFICER (pre-registration), General Surgery. Recognised F.R.C.S. Resident.

Applications to Hospital Secretary.

ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. BIRCH HILL HOSPITAL. SENIOR HOUSE OFFICER (obstetrics and gynæcology) required mid-September. The post is for 12 months in the first instance and is recognised for the D.Obst.R.C.O.G.

Apply at once to the Group Secretary, Central Offices, Birch Hill Hospital, Rochdale.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) RESIDENT HOUSE PHYSICIAN (Male) required early in September, 1956. Post not approved for pre-registration purposes.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

SALISBURY GENERAL HOSPITAL. Applications are invited for the appointment of RESIDENT HOUSE SURGEON/OBSTETRIC AND GYNÆCOLOGICAL HOUSE SURGEON (recognised by R.C.O.G.) to run consecutively in this order from 2nd November, 1956, for a period of 6 months in each post. The posts are open to pre-registration candidates.

Apply, enclosing 2 recent references, to Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital, Salisbury.

SALISBURY GENERAL HOSPITAL. Orthopædic Department. Applications are invited for the post of SENIOR HOUSE OFFICER (resident) or RESIDENT HOUSE SURGEON which is also recognised for pre-registration candidates. The Department has over 50 Beds and a large outpatient turnover, dealing with fractures and all types of orthopædic surgery.

Applications, stating age, nationality, qualifications and experience, and naming 2 referees, to the Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital, Salisbury, as soon as possible.

SCARBOROUGH HOSPITAL. (General—190 Beds.) Applications are invited for the post of NON-RESIDENT CASUALTY OFFICER (Junior Hospital Medical Officer) to commence duty approximately 1st November, 1956. Terms and conditions of service in accordance with those prescribed for medical and dental staffs. A furnished cottage is available for the successful applicant in the grounds of Cross Lane Hospital (1 mile distant), for which the present rent is £7 19s. 9d. per month.

Applications, giving age, qualifications, details of present and previous appointments, and the names of 2 referees, should be forwarded to the Hospital Secretary.

SKIPTON (near). GRASSINGTON HOSPITAL. (208 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER required for the above Hospital, which provides treatment for tuberculosis patients, men and women. Accommodation available for single applicants. Post tenable from 1st September, 1956.

Applications to Medical Superintendent.

SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL. SENIOR HOUSE OFFICER (Department of Obstetrics and Gynæcology) required. Post vacant 29th September. Preference given to applicants with general and obstetric experience.

Applications, with names of 2 referees, to Hospital Secretary, by 21st September, 1956.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of SENIOR REGISTRAR in Ophthalmology in the Professorial Unit at the Royal Infirmary of Edinburgh, vacant on 1st December, 1956.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 3 referees, should be sent to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, by 6th October, 1956.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of REGISTRAR in Radiotherapy at the Royal Infirmary and the Western General Hospital, Edinburgh.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 2 referees, should be submitted to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 6th October, 1956.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the post of MEDICAL REGISTRAR to the Edinburgh Geriatric Service based on the Longmore Hospital, Edinburgh.

Applications, giving particulars of age, qualifications and previous experience, together with the names of 2 referees, should be sent to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 6th October, 1956.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a REGISTRAR in Surgery at the Dunfermline and West Fife Hospital. The Hospital has 117 surgical beds, including those for E.N.T., ophthalmology and gynæcology.

Applications, giving particulars of age, qualifications and previous experience together with the names of 2 referees, should be sent to the Secretary, South-Eastern Regional Hospital Board, Scotland, 11, Drumsheugh-gardens, Edinburgh, 3, by 6th October, 1956.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. Anæsthetics. PERTH AREA. Applications are invited for the post of REGISTRAR in Anæsthetics in the Perth Area based on Perth Royal Infirmary (272 Beds) and Bridge of Earn Hospital (806 Beds). Living-in accommodation available at Bridge of Earn Hospital. Salary and conditions of service in accordance with national agreement.

Further particulars and forms of application from the Secretary to the Board, "Braeknowe," 430, Blackness-road, Dundee, with whom applications must be lodged not later than 29th September, 1956.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. PSYCHIATRIC UNIT, MARYFIELD GENERAL HOSPITAL AND DUNDEE ROYAL MENTAL HOSPITAL. Applications are invited for the post of REGISTRAR. These active Units (including a new E.E.G. Department) and their associated Outpatient Department are principally concerned with the treatment of neuroses and early psychoses and provide a comprehensive training in psychiatry. Candidates must possess, in addition to psychiatric experience, up-to-date knowledge of internal medicine. Salary and conditions of service in accordance with national agreement.

Further particulars and form of application from the Secretary of the Board, 430, Blackness-road, Dundee, with whom applications must be lodged not later than 22nd September, 1956.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. Radiodiagnosis. DUNDEE TEACHING HOSPITALS. Applications are invited for an appointment as SENIOR REGISTRAR in Radiodiagnosis at Dundee Royal Infirmary (510 Beds), and Maryfield Hospital, Dundee (370 Beds), both general teaching hospitals associated with the University of St. Andrews. Possession of the Diploma in Radiology is essential. A new Radiodiagnostic Department at Dundee Royal Infirmary has recently been brought into operation. Salary and conditions of service in accordance with national agreement.

Forms of application and further particulars from the Secretary to the Board, 430, Blackness-road, Dundee, with whom applications must be lodged not later than 29th September, 1956.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance :—

REGISTRAR in General Medicine based at the Royal Infirmary, Glasgow, with duties for a period at Belvidere I.D. Hospital, Glasgow.

REGISTRAR in Psychiatry based at the Southern General Hospital, Glasgow.

REGISTRAR in Anæsthetics based at Stobhill General Hospital, Glasgow.

These appointments are subject to the National Health Service (Scotland) superannuation regulations.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 29th September, 1956.

SHEFFIELD. CITY GENERAL HOSPITAL. (652 Beds. Recognised for training for the F.R.C.S. examination.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT REGISTRAR (orthopædics) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 24th September, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT SENIOR SURGICAL REGISTRAR (transitional appointment) required at City General Hospital, Sheffield, for 1 year in first instance. The successful candidate to reside at the Hospital when "on call." Applications invited from Senior Surgical Registrars in their fourth or subsequent years and from those who held such posts for 3 years or more but vacated them after 1st January, 1951.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 1st October, 1956, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications are invited for the following posts :—

(*a*) NON-RESIDENT REGISTRAR in Ophthalmology, Royal Infirmary.

Closing date for applications, 22nd September, 1956.

(*b*) RESIDENT HOUSE PHYSICIAN to the Professorial Unit, Children's Hospital. Vacant on 1st November, 1956 (6 months).

Closing date 26th September, 1956.

Applications for the above posts should give the names of 3 referees and be sent to :—

For post (*a*) : The Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1.

For post (*b*) : The Superintendent, Children's Hospital, Western Bank, Sheffield, 10.

SHREWSBURY. CROSS HOUSES HOSPITAL. (34 maternity beds.) OBSTETRIC HOUSE SURGEON (pre-registration post), vacant immediately.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY. (216 Beds.) HOUSE PHYSICIAN (pre-registration or otherwise), vacant 1st November, 1956.

Applications, with copy testimonials, to Group Secretary, Royal Salop Infirmary, Shrewsbury.

SIDCUP AND SWANLEY HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (casualty and orthopædic) required from 1st November, 1956. The successful applicant will serve 3 months as Casualty Officer and 3 months in the Orthopædic Department. The post is recognised under the Fellowship regulations as a period of 6 months casualty training.

Applications, stating age, qualifications, and experience, together with names and addresses of 2 referees, should be sent to Secretary, Queen Mary's Hospital, Sidcup, Kent.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) HOUSE PHYSICIAN (House Officer grade), required for duties mainly in the Pædiatric Department. Post vacant 1st October, 1956. Preference given to candidates seeking pre-registration posts under the Medical Act, 1950.

Applications to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

STAFFORD HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (anæsthetics), Male or Female, resident. Recognised for D.A.

Applications to Group Secretary, Stafford Hospital Management Committee, 13, Foregate-street, Stafford.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for 2 appointments as Whole-time REGISTRARS in Psychiatry to fill vacancies in the approved trainee establishment at Oakwood Hospital, Maidstone, Kent. Previous experience in general medicine is desirable. The appointments will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 29th September, 1956.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Pædiatrics (non-resident) to fill a vacancy in the approved hospital establishment at the Brighton and Lewes Group of hospitals, available on 1st December. The post is based on the Royal Alexandra Hospital for Sick Children, Dyke-road, Brighton, 1 (130 Beds), but duties will include the care of newborn babies at the Sussex Maternity Hospital, the Brighton General Hospital and Cuckfield Hospital. A higher qualification or special diploma would be an advantage. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 29th September, 1956.

SOUTH ELMSALL. WARDE-ALDAM HOSPITAL. Applications are invited for the post of RESIDENT SURGICAL OFFICER (Senior House Officer grade). Warde-Aldam Hospital is a general hospital of 39 Beds (general and orthopædic surgery and E.N.T.). Furnished flat available. The appointment is of attraction to surgeons reading for Fellowship.

Applications, giving details of qualifications and previous experience, with names of 2 referees, to be forwarded to—

D. G. DAVIES, Group Secretary.

Great Northern House, Salter-row, Pontefract, Yorks.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (278 Beds.) ORTHOPÆDIC HOUSE SURGEON required. Post recognised for Pre-registration Service and tenable for 6 months. The Hospital is the centre to which all trauma from a large industrial town and port is directed thus providing excellent experience in the treatment of traumatic conditions; patients with orthopædic conditions are also drawn from a wide area.

Applications, with copies of testimonials, should be sent as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL (274 Beds) and SOUTHAMPTON GENERAL HOSPITAL (472 Beds). SENIOR HOUSE OFFICER (E.N.T.) required beginning of October. This post is recognised for the F.R.C.S. (Eng.) and D.L.O. examinations and provides experience in all branches of E.N.T. work. The Group includes a diagnostic and distributing Hearing Aid Centre.

Applications, with copies of recent testimonials, should be forwarded as soon as possible, to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

STOCKTON-ON-TEES. SEDGEFIELD GENERAL HOSPITAL, SEDGEFIELD. (336 Beds.) SEDGEFIELD HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER ANÆSTHETIST urgently required. Full Consultant staff employed, and the post, which offers excellent facilities for anæsthetic training, is recognised for the higher qualifications. **Furnished Bungalow available at very moderate rental.**

Applications, together with 2 testimonials or names of 2 referees, to the undersigned as soon as possible.

L. WATSON, Group Secretary.

STOCKTON-ON-TEES. THE CHILDREN'S HOSPITAL, Durham-road, STOCKTON-ON-TEES. (84 Beds.) CLEVELAND HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER. The appropriate salary and conditions of service being in accordance with the Ministry of Health regulations.

Applications, with copies of 2 recent testimonials, should be forwarded to the undersigned at West Lane Hospital, Middlesbrough, as early as possible.

L. BRITTAIN, Group Secretary.

SUTTON, SURREY. BANSTEAD HOSPITAL. Applications are invited for the post of Locum Tenens SENIOR PSYCHIATRIC REGISTRAR from 15th October, 1956, to 17th February, 1957. Accommodation available for single person, charge for full residential amenities £3 16s. 9d. a week. Salary £24 per week.

Applications should be sent to the Physician-Superintendent.

SUTTON AND CHEAM HOSPITAL, Cotswold-road, SUTTON, SURREY. (146 Beds.) SURGICAL REGISTRAR. Candidates may visit Hospital by prior arrangement with Secretary (Tel.: Vig. 8691).

Forms of application, returnable by 29th September, obtainable from the Group Secretary, St. Helier Hospital, Carshalton, Surrey.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. (854 Beds.) HOUSE OFFICER (general surgery), vacant now Pre-registration post. Hospital recognised for F.R.C.S.

Detailed applications with copy testimonials to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. (845 Beds. Recognised for F.F.A.R.C.S. and D.A.) STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER in Anæsthetics. Post vacant 1st October, 1956. Previous anæsthetic experience desirable but not essential. The post offers experience in anæsthesia for all types of general surgery, thoracic and cardiac surgery, including an Obstetric Unit of 60 Beds. Staff includes a Senior Registrar who shares in emergency duties.

Applications, with necessary details and copy testimonials, to the Group Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. HOUSE OFFICER (general surgery) required. Pre-registration post. Hospital recognised for F.R.C.S.

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

SUNDERLAND. ROYAL INFIRMARY. (300 Beds.) HOUSE OFFICER (Male) required for duties in Gynæcological and Urological Units. Post vacant 26th September, 1956. Provisionally registered practitioners may apply.

Applications, naming 2 referees, to the Hospital Secretary, Royal Infirmary, Sunderland.

SWINDON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications invited for the appointment of SENIOR HOUSE OFFICER as Casualty Officer and Orthopædic House Surgeon at Great Western Hospital, Swindon. Post recognised by R.C.S. for 6 months of years training under Fellowship regulations. Work of Accident and Orthopædic Department, associated with Nuffield Orthopædic Centre (Wingfield Morris Orthopædic Hospital), Oxford, includes large number of industrial injuries. Salary £745 p.a., less £150 p.a. for residential emoluments.

Full details and names of 3 referees, to Secretary, 7, Okus-road, Swindon, Wilts, by 20th September.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. RESIDENT MEDICAL REGISTRAR required November.

Application forms from, and returnable to, Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor, by 30th September.

TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. 2 SENIOR HOUSE OFFICERS (anæsthetics) required for the Tees-side Group of hospitals, 1 post vacant now and 1 vacant 15th October. The Group is recognised for the F.F.A.R.C.S. and D.A. Facilities are available for postgraduate study and emergency work is by rota.

Applications, with copies of 3 testimonials, to—

Dr. J. G. WARNOCK.

North Ormesby Hospital, Middlesbrough.

TORQUAY. TORBAY HOSPITAL. Resident Senior HOUSE OFFICER (surgery) required early September, 1956. Post recognised for F.R.C.S. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, age, nationality, with copies of testimonials (quoting Ref. F. 955/72) to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY. (387 Beds.) Applications invited for post of RESIDENT ANÆSTHETIST (Senior House Officer), vacant 1st November. Post tenable for 12 months in the first instance and recognised for the D.A. and F.F.A.R.C.S. National Health Service salary, less £150 p.a. for residence.

Apply, stating age, qualifications and experience, together with 3 testimonials, to the Group Secretary, Tunbridge Wells Group Hospital Management Committee, Sherwood Park, Pembury-road, Tunbridge Wells.

WAKEFIELD. STANLEY ROYD HOSPITAL. Applications invited for post of JUNIOR HOSPITAL MEDICAL OFFICER in Psychiatry. Salary scale £775–£50–£1075. Married accommodation may be available.

Address written applications, giving full personal particulars, details of training, experience, &c., together with 2 names and addresses for reference, to W. BOWRING, Group Secretary.

Victoria Chambers, Wood-street, Wakefield.

AMENDED

WALLINGFORD (near), BERKSHIRE. FAIR MILE HOSPITAL. BERKSHIRE MENTAL HOSPITALS MANAGEMENT COMMITTEE. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER at above Mental Hospital of 1053 Beds. The post provides an excellent opportunity for postgraduate training in psychiatry, including outpatient clinic work and every facility is provided for study for the D.P.M. Suitable accommodation for a married man is available. The appointment is subject to the terms and conditions of service for hospital medical staff, the salary being £775–£50–£1075 p.a.

Applications, including details of age, qualifications and experience, together with the names of 2 referees, should be forwarded to the Medical Superintendent, Fair Mile Hospital, near Wallingford, Berks, within 10 days of the appearance of this advertisement.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens REGISTRAR in Thoracic Medicine required Llangwyfan Hospital immediately for approximately 3 months.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

WATFORD. SHRODELLS HOSPITAL. (General Hospital—420 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER to the Geriatric Unit. This unit of 180 Beds under full-time Geriatrician, offers excellent clinical experience in the diagnosis and treatment of acute and other illnesses in the elderly. Full laboratory and radiological facilities available. Adequate time for reading.

Applications, together with copies of not more than 2 testimonials, to reach the Medical Officer-in-charge as soon as possible.

WIGAN. ROYAL ALBERT EDWARD INFIRMARY. (200 Beds.) SENIOR HOUSE OFFICER in Orthopædic Surgery. Post vacant 1st November.

Applications to Secretary.

WINDSOR. KING EDWARD VII HOSPITAL. Obstetric AND GYNÆCOLOGICAL HOUSE SURGEON required, Male or Female, for post vacant 1st October. Post recognised for M.R.C.O.G. and D.Obst.R.C.O.G. Not a pre-registration post. Successful candidate will be resident, at the Old Windsor Unit of this Hospital. Applicants required to be members of a Medical Protection Society.

Applications, stating age, nationality, qualifications, with dates, with copies of recent testimonials or names of 3 referees, to Hospital Secretary, as soon as possible.

IBADAN, NIGERIA. UNIVERSITY COLLEGE HOSPITAL. Applications are invited from fully qualified medical practitioners for the posts of SENIOR REGISTRAR (1) and REGISTRARS (2) in Pathology.

Salary—

Senior Registrar: First tour £1428 p.a.; second tour £1482 p.a.; third tour £1542 p.a.; fourth tour £1596 p.a.; plus inducement addition of £300 p.a. for expatriate Senior Registrar.

Registrars: First tour £1164 p.a.; second tour £1212 p.a.; plus inducement addition of £270 for expatriate Officers.

Gratuity: On satisfactory completion of agreement a gratuity of £37 10s. will be paid for each completed period of 3 months service.

Outfit allowance: An allowance of £60 will be made on first appointment.

Duration of appointment—

Senior Registrar: 1 tour of 12 months in the first instance, renewable by mutual agreement for further tours of 12 months—to a maximum of 4 tours.

Registrars: 1 tour of 12 months in the first instance, renewable by mutual agreement for a further tour of 12 months.

Leave: Expatriate Officers will be eligible for 7 days leave in the United Kingdom on full pay, for each completed month of service.

Passages: Free first-class passages to and from Nigeria are provided for expatriate doctors and their wives on first appointment, annual leave and on completion of agreement. Free first-class passages to Nigeria will be provided for Nigerian doctors and their wives.

Children's allowances and passages: Officers will be eligible for children's allowances and passages in accordance with existing regulations.

Quarters: Partly furnished quarters are provided at a rental of 8½% of salary, excluding inducement addition.

Superannuation: Arrangements can be made to enable doctors to continue their National Health Service superannuation scheme contributions, details of the revised salary and gratuity payable in such cases can be obtained on application to the London Office.

Applications should be submitted not later than 28th September, 1956, on the appropriate forms, which can be obtained with further particulars on receipt of an addressed foolscap envelope, from the Adviser on Staff Recruitment, London Office, University College Hospital, Ibadan, 57, Catherine-place, London, S.W.1.

Public Appointments

DUBLIN. LOCAL APPOINTMENTS COMMISSION. Position vacant. SURGEON, Tipperary (S.R.) co. Council. Salary: £1517, with permission to engage in private practice, plus the use of certain beds.

Application forms and particulars from the Secretary, Local Appointments Commission, 45, Upper O'Connell-street, Dublin. Latest time for receiving completed application forms, 5 P.M. on 28th September, 1956.

DURHAM. ADMINISTRATIVE COUNTY OF DURHAM. BOROUGH OF HARTLEPOOL. Applications are invited from duly qualified medical practitioners (Women) holding a Degree or Diploma in Sanitary Science, Public Health, or State Medicine for the separate appointments of ASSISTANT WELFARE MEDICAL OFFICER (Maternity and Child Welfare) AND MEDICAL OFFICER OF HEALTH for the Municipal Borough of Hartlepool. The total salary payable will be £1241 7s. 3d. rising by 3 increments of £53 3s. 8d., 1 increment of £57 10s. 0d. and 4 increments of £47 10s. 0d. to £1648 8s. 3d. p.a. The appointments will be superannuable. Canvassing, directly or indirectly, will disqualify and applicants must disclose whether they are related to any member or senior officer of the employing authorities.

Further particulars of the appointment and form of application may be obtained from the undersigned. Applications, giving the names of 3 persons to whom reference may be made, should be sent to the Clerk of the County Council not later than 1st October, 1956. J. K. HOPE, Clerk of the County Council.

Shire Hall, Durham.

L. O. WILLIAMS, Town Clerk.

Town Clerk's Office, Hartlepool.

FACTORY DOCTORS. Factories Acts, 1937 and 1948. The following appointments as Appointed Factory Doctor are vacant. Apply to Chief Inspector of Factories, 19, St. James's-square, London, S.W.1.

District	*County*	*Latest date for receipt of applications*
PLYMOUTH WEST ..	DEVON ..	29TH SEPTEMBER, 1956
NEWBURY	BERKS ..	29TH SEPTEMBER, 1956

HER MAJESTY'S OVERSEA SERVICE. Nigerian FEDERAL GOVERNMENT SERVICE.

(1) PATHOLOGIST (hæmatology) required to develop existing basic scheme for Blood Transfusion Centre at Yaba and conduct research into the blood-group systems of West Africans and other related problems.

(2) PATHOLOGISTS required to carry out routine hæmatology, chemical pathology, morbid anatomy and to train laboratory technicians. There are also opportunities and facilities for individual research in clinical pathology. Experience in pathology required.

Candidates must possess medical qualification registrable in United Kingdom. A higher qualification (e.g., D.C.P. or Dip. Bact.) would be an asset.

Appointments may be made:

(*a*) On 3 years probation for permanent and pensionable employment. Pension (non-contributory) at the rate of 1/600th of final pensionable emoluments for each completed month of reckonable service.

(*b*) From National Health Service. Candidates may leave National Health Service but retain their superannuation rights up to 6 years and receive a gratuity (taxable) of 20% of aggregate of their salary. Salaries under (*a*) or (*b*) range from £1128 to £1950 p.a.; or

(*c*) On short-term contract (2 tours each of 18–24 months) with salary of £1338–£2286. Gratuity (taxable) of £37 10s. for each completed period of 3 months service (including leave).

Officers appointed under (*a*) or (*c*) are required to contribute to a Widows' and Orphans' Pension Scheme.

Quarters at low rental. Free return passages for Officer and wife. Return passages for children, to age 18, provided this does not exceed cost of 2 adult return passages in any 1 tour of service. Children's (Separate Domicile) allowance of £75 a year for each child under 18, ceasing if children join parents in Nigeria. Income-tax at low local rates. Local leave permissible and generous home leave after each tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting No. BCD. 117/14/05).

LEICESTER. CITY OF LEICESTER. Applications are invited from registered medical practitioners for the appointment of SCHOOL MEDICAL OFFICER AND ASSISTANT MEDICAL OFFICER OF HEALTH. The duties will consist mainly of School Health Service and maternity and child welfare work. Salary, in accordance with the national scale, will be £1050–£1475 p.a. Previous experience in a similar capacity will be taken into consideration in determining the commencing salary. The appointment will be superannuable and subject to termination by 3 months notice.

Full details of the appointment may be obtained from the undersigned to whom applications should be sent, on the official form, within 14 days of the appearance of this advertisement.

E. K. MACDONALD,
Medical Officer of Health and Principal School Medical Officer.
Grey Friars, Leicester.

STAFFORDSHIRE COUNTY COUNCIL. Biddulph URBAN DISTRICT COUNCIL; LEEK URBAN DISTRICT COUNCIL. Applications are invited for the separate part-time appointments of ASSISTANT COUNTY MEDICAL OFFICER AND SCHOOL MEDICAL OFFICER, MEDICAL OFFICER OF HEALTH of the Biddulph Urban District and MEDICAL OFFICER OF HEALTH of the Leek Urban District. The appointments together will constitute whole-time, the allocations being 5 half-days, 3 half-days and 3 half-days, respectively. The proportionate salary for each appointment is calculated in accordance with the latest agreed scale, and increments will be given for previous service in the same capacity, the ranges being:—

County Council—
£596 11s. 10d.–£28 8s. 2d. (3)–£31 5s. 0d. (5)–£838 1s. 4d.
Biddulph Urban District Council—
£501 16s. 4d.–£15 (4)–£561 16s. 4d.
Leek Urban District Council—
£501 16s. 4d.–£15 (4)–£561 16s. 4d.

A car is necessary and an allowance will be paid.

The posts are superannuable, and the successful candidate must pass a medical examination and produce his birth certificate. Applicants must be fully qualified medical practitioners with experience in public health duties, and must hold the Diploma of Public Health or its equivalent. The candidate appointed will, as regards the County Council duties, act under the direction of the County Medical Officer of Health, and will be required to perform such duties as may from time to time be prescribed. As regards the duties of Medical Officer of Health, he will be subject to the Sanitary Officers (Outside London) Regulations, 1935 and 1951, and to the sole control and direction of the Urban District Councils. The County Council appointment will be subject to 3 calendar months notice in writing on either side.

Forms of application may be obtained from the County Medical Officer of Health, County Buildings, Stafford, and should be returned to him not later than by first post on 2nd October, 1956.

T. H. EVANS, Clerk of the County Council.
R. W. TRACE, Clerk of the Biddulph U.D.C.
S. F. ESLAND, Clerk of the Leek U.D.C.

County Buildings, Stafford, 10th September, 1956.

BIRMINGHAM. CITY OF BIRMINGHAM EDUCATION COMMITTEE. Applications are invited from registered medical practitioners (Men or Women) for appointment as SCHOOL MEDICAL OFFICER in the School Health Service. The possession of a D.P.H. or D.C.H. will be an advantage. Salary in accordance with Whitley Council scale of £1050–£50–£1200–£55–£1475 p.a. Appointment is subject to the appropriate superannuation act and to the passing of a medical examination.

Forms of application obtainable from the undersigned (stamped addressed envelope) must be returned not later than 6th October, 1956. Canvassing disqualifies.

E. L. RUSSELL, Chief Education Officer.
School Health Service, Queen's College Chambers,
38A, Paradise-street, Birmingham, 1.

BIRMINGHAM. CITY OF BIRMINGHAM. Public HEALTH DEPARTMENT. Applications invited from registered medical practitioners for post of ASSISTANT ADMINISTRATIVE MEDICAL OFFICER OF HEALTH (Male or Female). Candidates should hold the Diploma of Public Health. The successful candidate will have an opportunity to gain administrative experience in all branches of the Public Health Service, including maternity and child welfare. Salary scale £1405–£55–£1625 p.a. Commencing salary within the scale will depend upon the Medical Officer's experience. Pension scheme (including Widows and Orphans); medical examination. The Officer appointed will be required to devote his/her whole time to official duties and the appointment will be subject to 3 months notice on either side.

Applications, with the names of 3 persons to whom reference may be made, to be sent to the Medical Officer of Health, Council House, Birmingham, 3, not later than 24th September, 1956.

HER MAJESTY'S OVERSEA SERVICE. Kenya. Medical OFFICERS with qualifications registrable in United Kingdom required for general duties. Successful candidates may be posted to any station in Kenya. During earlier years of service an officer will be expected to carry out general medical and surgical duties including varying amount of public-health administration. In most stations, even if remote from the larger towns, it is possible to maintain interest in any particular branch of medicine or surgery, to which the officer is attracted. The work of every medical officer is based on a hospital which may vary in size and facilities from small district hospital, meeting needs of comparatively primitive community, to large and modern provincial hospital. Appointments can be made on permanent basis with pension (non-contributory), or on short-term contract with gratuity (taxable) payable on satisfactory completion of service. Normal retiring age is 55. Salary ranges from £1284 to £2115 a year, starting point determined by experience. 4 extra increments given to successful candidates possessing the F.R.C.S., M.R.C.P., D.P.H., or other approved higher qualifications. Permanent medical Officers are eligible to be considered at any time for promotion to super-scale posts in Kenya and other territories in medical administrations or, if they possess higher qualification and suitable experience, in specialist posts. Quarters at rental varying from £30 to £78 a year according to size and type, and furniture at rate varying from £15 to £36 a year. Free passages in both directions for Officer and wife and up to cost of 1 adult fare for children. Taxation at local rates. Annual local leave permissible and generous home leave granted after each tour of from 24 to 45 months. Educational facilities available.

Application forms from Director of Recruitment, Colonial Office, Great Smith-street, London, S.W.1 (quoting No. BCD. 117/7/02).

SOUTHERN GAS BOARD. Applications are invited for the new and pensionable post of Whole-time ASSISTANT MEDICAL OFFICER. Previous experience in industrial medicine would be an advantage. The salary will be on Senior Staff scale, Grade D, £1375–£1575, or Grade E, £1525–£1725, or by arrangement with the successful applicant. The successful candidate will be required to pass a medical examination and, unless already subject to a Pension Scheme by virtue of the Gas (Pension Rights) Regulations, 1950, will be required to join the Board's Staff Pension Scheme.

All applications must be made on a form which may be obtained from the Personnel Manager, Southern Gas Board, 164, Above Bar, Southampton, and completed forms should be returned by Monday, 22nd October, 1956.

P. VALON BENNETT, Personnel Manager.

THE REPUBLIC OF THE SUDAN. The Ministry of Health invite applications for the post of SURGICAL SPECIALIST. Candidates must possess the necessary professional qualifications—viz., F.R.C.S. or its internationally recognised equivalent. Age between 28 and 48. Salary range £E1750–£E2330 (for Junior Specialists) or a flat £E2330 for Specialists. Candidates for this post may apply for secondment from the National Health Service for a period of up to 3 years under the terms of the circular letter No. RHB/(52)106EG(52)101 of 30th September, 1952. The appointment will be on a short-term contract for a period up to 5 years. Starting salary will be determined according to age and qualifications. A bonus of 1 months salary for each completed year of satisfactory service will be payable and an outfit allowance of £E50 on signature of contract.

Further particulars and application form can be had on application to Dr. E. P. PRATT, 137, Harley-street, London, W.1.

SASKATCHEWAN DEPARTMENT OF PUBLIC HEALTH

CANCER CLINIC
UNIVERSITY HOSPITAL
SASKATOON, SASKATCHEWAN, CANADA

SENIOR CANCER CLINIC ASSOCIATE required for the above Clinic.

Salary $828 per month with automatic annual increases to $994 per month.

Requirements—Certification by the Royal College of Physicians and Surgeons of Canada or its equivalent. Applicant should be an Internist and have considerable experience in investigation and diagnosis of cancer cases.

For application forms or further information write Personnel Officer, Provincial Health Building, Saskatchewan Department of Public Health, Regina, Saskatchewan.

General Practice

For an Executive Council post (England and Wales) apply on form E.C.16A obtainable from the council. Mark envelope "Vacancy."

PORT MORESBY (PAPUA AND NEW GUINEA). LOCUM required for 6 months from mid-October with possibility of taking over practice, which includes some midwifery. £150 (sterling) tax-free, and all found, plus half air fare. Interview in London.—Apply with brief particulars: Address, No. 244, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Hospital Services : Non-Medical Appointments

BIRMINGHAM, 15. THE QUEEN ELIZABETH HOS-PITAL. BIOCHEMIST (Basic grade) required for the Biochemical Laboratory at above Hospital. Candidates must hold a University degree in Science or the Associateship of the Royal Institute of Chemistry. Salary according to Whitley Council scale with allowances for postgraduate study or experience.

Applications to be sent as soon as possible to House Governor, the Queen Elizabeth Hospital, Edgbaston, Birmingham.

SOUTH AFRICA. PROVINCIAL ADMINISTRATION OF THE CAPE OF GOOD HOPE. HOSPITALS DEPARTMENT. Hospital Service: Vacancy. Groote Schuur Hospital, Observatory, Cape Town; Technician (Grade B) (E.E.G. Technician-Recordist): Departments of Neuro-psychiatry and Neuro-surgery: Electro-encephalography Laboratory.

(1) Applications are invited from suitably qualified persons for appointment to the post of TECHNICIAN (Grade B) (E.E.G. Technician-Recordist) at the Groote Schuur Hospital, Observatory, Cape Town, with salary on the scale of £750–£36–£894 p.a.

(2) In addition to the salary scale indicated a non-pensionable cost-of-living allowance of £234 p.a. is payable to a married whole-time male official.

(3) Candidates must give full particulars in regard to their training, qualifications, and experience, for example, the places and dates of training, details and dates of qualifications, and the periods and institutions where experience has been gained, and must also state the earliest date on which they can assume duty.

(4) Application must be made on the prescribed form, Staff 23, which, together with details as regards conditions of service and transport facilities, is obtainable from the Staff Clerk, Room 309, South Africa House, Trafalgar-square, London, W.C.2.

(5) The completed application forms must be addressed to the Director of Hospital Services, P.O. Box 2060, Cape Town, South Africa, and must reach him not later than 20th October 1956.

Miscellaneous

Shell Petroleum Company Limited invites applications from suitably qualified medical practitioners for the post of Medical Officer for general duties. Candidates should be 30–35 years of age, have had at least 4 years experience in hospital appointments, general practice, or with H.M. Forces, and must be willing to serve in the Company's medical establishments both in the U.K. and overseas. Previous industrial or overseas experience is not essential. The salary of the successful applicant will be based on experience and he will be eligible for membership of Pension Fund.

Please write in confidence to: Staff Department (R), Shell Petroleum Company Ltd., 16, Finsbury-circus, London, E.C.2.

Cameroons Development Corporation require for service in the British Cameroons under United Kingdom Administration a Medical Officer. Candidates should have a good experience of general medical and health work and preference will be given to those who either possess a Diploma in Tropical Medicine or who have had tropical experience. The work generally consists of general medical and health supervision of all personnel in large plantations but offers opportunity for surgery. Commencing salary £1525 p.a. rising by annual increments of £50 to £1975. First-class passages are provided for Officers and their wives, together with free quarters and heavy furniture during residence in the Cameroons. A reasonable amount of free lighting and fuel is also provided, and necessary transport. An outfit allowance of £80 is payable on first appointment. Children's allowances at the rate of £75 each are payable up to a maximum of 2. Officers are required to contribute 10% of their salary to a provident fund to which the Corporation contributes a further 15%. Tours of about 18 months with 1 weeks leave on full pay for each month of service if the Officer is returning otherwise half this amount of leave.

Applications, giving particulars in writing, to RUBBER & MINING AGENCIES LIMITED, MO, 52, Leadenhall-street, London, E.C.3.

Nurse Receptionist requires post London, mornings. —Address No. 245, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

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Hypnotism. Will all Doctors interested in this subject for Medical purposes please write to the Secretary, British Society of Medical Hypnotists, 126, Harley-street, W.1.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimen of urine and £1 1s. fee. Haematology, Biochemistry. Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Applicants for posts requiring testimonials copied or duplicated should communicate with MANTON SECRETARIAL SERVICE LTD., 98, Victoria-street, S.W.1 (Phone: VICtoria 0141), who are specialists in this kind of work.

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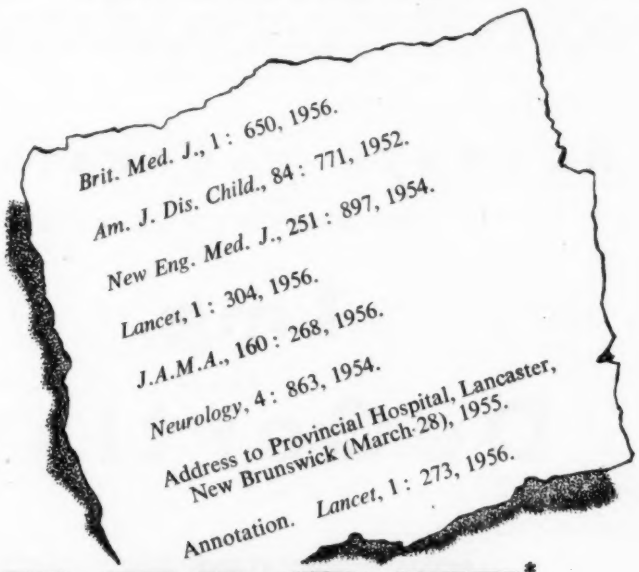
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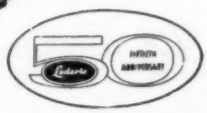

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